Contingent Value Rights on the Rise in Life Sciences and Healthcare M&A

A case study of how Lilly's CVR sweetened the Sigilon Acquisition

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Laymen's summary

Consider the scenario of a large pharmaceutical company trying to buy a smaller pharmaceutical company. To make this deal happen, the buyer and seller need to agree on the price of the smaller biopharmaceutical company. Both the buyer and seller would hire a financial adviser to estimate the 'fair' price of the company. Of course, the buyer wants to pay as little as possible, whereas the sellers wants to get as much money as they can. When the buyer and the seller have very different ideas about the value of the company, a so-called 'valuation gap' exists. If the two companies do not reach an agreement, the deal might not happen. But here is the interesting part: there might be a way to bridge this gap.

Let's take an example: a small pharmaceutical company is developing a promising new drug. Before the company is allowed to sell this drug, they must test it in multiple clinical trials to prove that the drug is safe and effective. Now, for some reason, the management of this small company decides they want to sell it. The management team and their financial advisers believe that the company is worth $100 million. On the other side, there is a large pharmaceutical company that is interested in buying the small company. They think that, if the new drug works, it could help a lot of patients. However, the management of the large pharmaceutical company is a bit skeptical about safety of this drug. They only want to pay $60 million. This creates a valuation gap: there is a difference of $40 million between what the buyer is willing to pay and what the seller thinks it is worth. Now, they could try to negotiate with the help of financial advisers, but reaching an agreement is not very likely in this situation.

The management teams have the option to enter into a special contract known as a Contingent Value Right (CVR). A CVR is an agreement between to companies that says: If certain future events happen as expected, the buyer will make an additional payment to the seller. If these event do *not* happen, the buyer will not have to pay extra. In our example, let's say the two management companies agree to a CVR. This means that if the drug passes all the safety and efficacy tests, the large pharmaceutical company will have to pay an addition $40 million to the seller. However, if the drug does not pass these tests, the seller will not get anything more than the $60 million it already received.

In this study, we elaborate on why more and more American pharmaceutical companies decide to include these CVRs as part of the deal, we clarify the situations in which they are particularly useful, and we describe how financial advisers can respond to this trend.

Executive Summary

Background | Financial advisers in the field of life sciences and healthcare M&A observed an apparent upward trend in the use of a unique form of payment called Contingent Value Right (CVR). In the context of public Mergers & Acquisitions (M&A), CVRs are contractual agreements in which the buyer commits to paying an additional consideration to the seller when specific payment triggers are met. Upon further research, multiple sources either confirmed or anticipated the increase in the use of CVRs, particularly within the life sciences and healthcare industry in the United States (Golden & Hanks, 2023; KPMG, 2023; Miller, 2023; Wagner Partin et al., 2023). Over the past decade, the average number of M&A transactions including a CVR, across all industries, was roughly 6 per year. However, in the first months of 2023 alone, the life sciences sector witnessed at least four public acquisitions with a CVR as part of the deal structure (AstraZeneca, 2023; Becker, 2023; Ipsen, 2023; Satsuma Pharmaceuticals, 2023). Interestingly, this trend appears to be quite notable in the United States while being completely absent in Europe.

Research questions | In this research, the primary objective was to address the knowledge gaps related to the apparent upward trend CVRs in biopharma deal structures. We aimed to uncover underlying reasons driving this trend and to discern the factors contributing to their frequent use in the United States compared to Europe. Furthermore, we set out to identify the specific situations in which CVRs prove to be particularly valuable. Our ultimate goal was to gather insights and formulate recommendations for the financial advisers at Van Lanschot Kempen.

Relevance | Knowledge of emerging instruments such as CVRs is essential for staying competitive in the highly specialized field of financial advisory. More specifically, clients in the life sciences and healthcare sector look for advisors with both financial expertise and industry-specific knowledge. In the end, this report will assist financial advisers at Van Lanschot Kempen in providing 'personal', 'specialized', and 'entrepreneurial' solutions to their clients, in line with three of their four core values.

Methods | This study used literature research and expert interviews to gain insights into the trends shaping the use of CVRs in the broader biopharma M&A industry. In addition, a case study of the Lilly-Sigilon acquisition (June 29, 2023) was carried out (Eli Lilly & Company, 2023a). The reason to include a CVR in the deal structure is shaped by a variety of factors that may not always be readily apparent. Therefore, these factors should be assessed on a case-by-case basis. By using this combination of research methods, we managed to obtain insights into the use of CVRs at both the industry level and the company level.

Conclusion & recommendations | Based on our research, we have strong indications that the use of CVRs in biopharma deal structures will continue to increase. Moreover, once a legal precedent is set, we foresee that this trend will expand into Europe. We identified four reasons for a biopharma companies to include a CVR in their deal structure, namely to bridge a valuation gap, to mitigate risk, to sweeten the deal, or due to lack of alternative options. We recommend financial advisers to educate themselves on the structure and valuation of CVRs, two of the most complicated aspects of this instrument, and to engage legal professionals who understand the structure and applicability of CVRs in the European context

1. Introduction

Van Lanschot Kempen is a Dutch financial institution listed on Euronext Amsterdam (AMS: VLK) with a history dating back to 1737. Van Lanschot Kempen focuses on providing a range of financial services, one of which is Investment Banking (Van Lanschot Kempen, 2023). The Investment Banking department provides various financial services, including advising on Mergers & Acquisitions (M&A), assisting corporates in raising capital, and conducting equities research. What sets Van Lanschot Kempen apart is the strategic structuring of its Investment Banking department into specialized teams, each dedicated to specific sectors, namely European Real Estate, Life Sciences & Healthcare, Infrastructure & Renewables, and Tech & Fintech. Within each of these sectors, Van Lanschot Kempen provides expert knowledge and tailored solutions for their clients (Van Lanschot Kempen, 2023). During the process of preparing for this research, I had the opportunity to engage in conversations with several professionals from the Corporate Finance Life Sciences & Healthcare team at Van Lanschot Kempen. These discussions revealed a recurring and interesting subject.

Several professionals within the Corporate Finance Life Sciences and Healthcare team at Van Lanschot Kempen, had noticed an apparent upward trend in the use of an instrument called Contingent Value Rights (CVRs). CVRs represent a unique form of payment to bridge so-called valuation gaps in the context of public M&A (Kirman, Goldfeld & Timaru, 2011). They are contractual agreements in which the buyer commits to paying an additional cash- or stock-based consideration to the seller when specific payment triggers are met. The industry professionals pointed out that, in the first months of 2023, at least four public acquisitions were announced with a CVR as part of the deal structure, including AstraZeneca's acquisition of CinCor Pharma, Ipsen's acquisition of Albireo Pharma, Assertio Holdings' acquisition of Spectrum Pharmaceuticals, and Shin Nippon's acquisition of Satsuma Pharmaceuticals (AstraZeneca, 2023; Becker, 2023; Ipsen, 2023; Satsuma Pharmaceuticals, 2023). Upon further research, multiple sources either confirmed or anticipated the increase in the use of CVRs, particularly within the life sciences and healthcare industry in the United States (Golden & Hanks, 2023; KPMG, 2023; Miller, 2023; Wagner Partin et al., 2023). In the life sciences and healthcare industry, CVR payments are typically triggered by the achievement of milestones related to drug development, regulatory approval, or sales (Wagner Partin et al., 2023). Upon the successful achievement of these predetermined milestones, CVR holders are entitled to receive these additional payments. Interestingly, the industry professionals also pointed out that CVRs are frequently used in life sciences and healthcare transactions in the United States, but rarely in European M&A deals.

The firsthand observations of the growing use of CVRs in the life sciences and healthcare field prompted a study into the following questions: 1) What are the reasons behind this trend? 2) Why are CVRs more often incorporated in deal structures in the US than in Europe? 3) What are the specific situations in which CVRs prove to be particularly valuable? 4) What does this emerging trend imply for financial advisers at Van Lanschot Kempen? To facilitate a thorough examination of CVRs in the life sciences and healthcare sector, this report is organized into several chapters.

First, this report will provide a brief overview of Van Lanschot Kempen, outlining the structure of its Investment Banking department and emphasizing its leading position in the European life sciences and healthcare industry.

Next, this research will delve into the industry dynamics and prevailing market conditions of the life sciences and healthcare industry. The aim is to develop a thorough understanding of the critical role of M&A in this industry, which will enable us to address questions related to the use of CVRs. In this chapter, key questions will be addressed, such as: 1) What are the defining characteristics of the life sciences and healthcare industry? 1) What role does M&A play in shaping this industry? 3) What are current trends influencing M&A in the life sciences and healthcare sector? 4) Are there trends that could explain the growing use of CVRs? Through this analysis, the goal is to provide a

solid foundation for comprehending the broader context in which CVRs are being employed and the factors driving their growing adoption.

In the third section of this study, the focus shifts towards an investigation of the practical use of CVRs within the life sciences and healthcare industry. The aim is to explore different aspects related to bridging valuation gaps, including methods for valuing biopharma companies, situations in which CVRs prove valuable, pros and cons associated with the use of CVRs, and potential legal barriers within the European system that may affect CVR utilization. Additionally, this chapter is complemented by incorporating insights from two industry professionals who share their perspectives on CVRs in the context of European life sciences M&A.

Lastly, to gain an in-depth understanding of CVRs and their real-world applications, a case study was conducted on a transaction with a CVR as part of the deal structure. Case studies are particularly valuable when investigating unique or relatively rare occurrences. Through such an analysis, one can derive insights that may be applicable to a broader context. This case study focuses on the acquisition of Sigilon Therapeutics by Eli Lilly & Company, a transaction announced on June 29, 2023 (Eli Lilly & Company, 2023a). Several factors make this acquisition an ideal case study choice for this report. First, it took place under the prevailing market conditions, in line with the research's main focus on revealing the reasons behind the apparent increase in the use of CVRs. Second, the transaction featured a CVR with notable characteristics, serving as an illustrative example of how these instruments are strategically employed within the life sciences industry.

By analyzing industry trends, investigating a real-world case, and drawing insights from professionals, this research aims to illuminate how CVRs can be a useful instrument for M&A in the life sciences and healthcare sector. Financial advisers should consider the study of instruments such as CVRs for several reasons. First, knowledge of emerging instruments is essential for staying competitive in the highly specialized field of financial advisory. Given that CVRs appear to be relatively uncommon in Europe, this research may provide an opportunity to gain a better understanding. Second, knowledge of this topic facilitates a client-centric approach. Clients in the life sciences and healthcare sector look for advisors with both financial expertise and industry-specific knowledge. By understanding CVRs and their growing role in this sector, financial advisers can employ them as tools in complex transactions, ultimately adding value to their clients' M&A strategies.

2. Methodology

The primary objective of this research was to examine the strategic use of CVRs within the current market landscape, focusing on their application in the life sciences M&A sector. Moreover, the study aimed to shed light on the advantages and drawbacks of using CVRs. To achieve this, a multi-faceted research approach was employed, involving the collection and analysis of data from different sources.

The first method used in this study was extensive literature research of reliable internet sources, academic articles, and industry reports. This approach focused on acquiring a deep understanding of the current M&A landscape within the life sciences industry (Chapter 4) and to analyze the upward trend in the use of CVRs (Chapter 5). A multitude of search terms were used to retrieve information from the search engines Google and Google Scholar. Search terms related to the life sciences M&A industry included a combination of the following: 'life sciences', 'healthcare', 'pharmaceutical industry', 'M&A', 'trends', '2023', 'financing', 'funding', 'dealmaking', etc. Moreover, search terms such as "EY", "McKinsey", "KPMG", etc. were added to uncover relevant industry reports, case studies, and expert insights from leading financial and strategic advisors. Search terms such as "CVR", "payment methods", "public M&A", "valuation gap", "life sciences", etc. were used in different combinations on Google and Google Scholar, to get a thorough understanding of CVRs in the life sciences industry.

To explore the context-dependent use of CVRs, a case study methodology was employed (Chapter 6). A case study method provides an in-depth exploration of CVRs in a real-world example, giving an idea of the negotiation dynamics and strategic decisions, and enriching the research with practical insights. For this research, the role of CVRs in life sciences and healthcare M&A was investigated through an analysis of the events and negotiations surrounding the acquisition of Sigilon Therapeutics by Eli Lilly and Company. The selection of the Sigilon Therapeutics and Eli Lilly case was based on several criteria, including its occurrence in the current market environment, the presence of a prominent CVR in the deal structure, and the data availability. Data for this case study were collected from a variety of publicly available documents, such as press releases, financial reports, and regulatory filings related to the acquisition. News sources such as FiercePharma were used to gauge market sentiment over time and Refinitiv Eikon was used to analyze share price data and analyst coverage.

To gain a more nuanced perspective, qualitative one-on-one interviews were conducted. Two key professionals, each with distinct expertise relevant to the study, were selected as interview participants. The first interviewee was a legal professional with expertise in public M&A transactions. This individual's insights were instrumental in understanding the legal complexities of CVRs within the context of European M&A. The second interviewee was a finance professional with a focus on life sciences M&A. Their knowledge provided a useful perspective on the practical aspects of employing CVRs in the life sciences and healthcare sector. Semi-structured interviews were conducted to allow for flexibility and in-depth exploration of key topics. The interviews were designed with open-ended questions to encourage participants to share their knowledge, experiences, and opinions (see Chapter 10). The interviews were recorded with consent and later transcribed for analysis. After the analysis, all recorded and transcribed materials were erased.

In combining these research methods, extensive literature research, a case study analysis, and expert interviews, this study ensured a comprehensive examination of the strategic use of contingent value rights within the current market conditions. Triangulating findings from different sources contributed to a holistic exploration of the subject, offering valuable insights into the advantages, drawbacks, and practical implications of using CVRs as a tool for bridging valuation gaps in the dynamic landscape of life sciences M&A.

3. Van Lanschot Kempen

Van Lanschot Kempen, founded in 1737 and headquartered in 's-Hertogenbosch, is the oldest independent financial institution in the Netherlands. As of September 4, 2023, Van Lanschot Kempen (AMS: VLK) has a market capitalization of €1.18bn, indicating an impressive year-to-date increase of +23.4%. With 1,780 full-time employees, Van Lanschot Kempen is committed to providing excellent service and expertise to its clients, achieving a net result of €84.3m in 2022 (Van Lanschot Kempen, 2023). Van Lanschot Kempen's purpose revolves around preserving and creating wealth for their clients and society in a sustainable manner. Their decision-making processes and interactions with clients are guided by their values: personal, specialized, entrepreneurial, and decisive. Strategically, Van Lanschot Kempen aims for sustainable and profitable growth while maintaining a capital-light balance sheet.

Van Lanschot Kempen's main business activities include Private Banking, Investment Management, and Investment Banking (see Figure 1). The Investment Banking department at Van Lanschot Kempen consist of two divisions, namely Securities and Corporate Finance. Van Lanschot Kempen's Securities division is located in Amsterdam, Antwerp, London, and New York, and consists of specialized teams focusing on sales, trading, and equities research. On the other hand, the Corporate Finance division is only located in Amsterdam and comprises teams engaged in M&A, Debt Advisory, and Equity Capital Markets. The Investment Banking department as a whole, is dedicated to four specific sectors in Europe, namely Real Estate, Life Sciences & Healthcare, Infrastructure & Renewables, and Tech & Fintech (Van Lanschot Kempen, 2023).

More specifically, Van Lanschot Kempen Investment Banking is a market leader within the European Life Sciences and Healthcare sector. The Corporate Finance Life Sciences & Healthcare team acted, for example, as sole financial advisor in the sale of Sanquin Reagents to Gilde Healthcare (Van Lanschot Kempen, 2022). Their role was to generate interest from strategic and financial buyers, and to execute the transaction. In addition, this team collaborates with the Equity Capital Markets team to aid Life Sciences and Healthcare companies with their IPOs, follow-on transactions, and other equity-linked transactions. To illustrate, Van Lanschot Kempen took on the role of Joint Global Coordinator and Joint Bookrunner in argenx's Euronext Brussels IPO in 2014, and later acted as Financial Adviser during its Nasdaq IPO in 2017 (Van Lanschot Kempen, 2014, 2017). All in all, Van Lanschot Kempen's continuous dedication to excellence in the European Life Sciences and Healthcare sector places them at the forefront, where they strive to stay on top of industry trends and deliver specialized expertise to their clients.

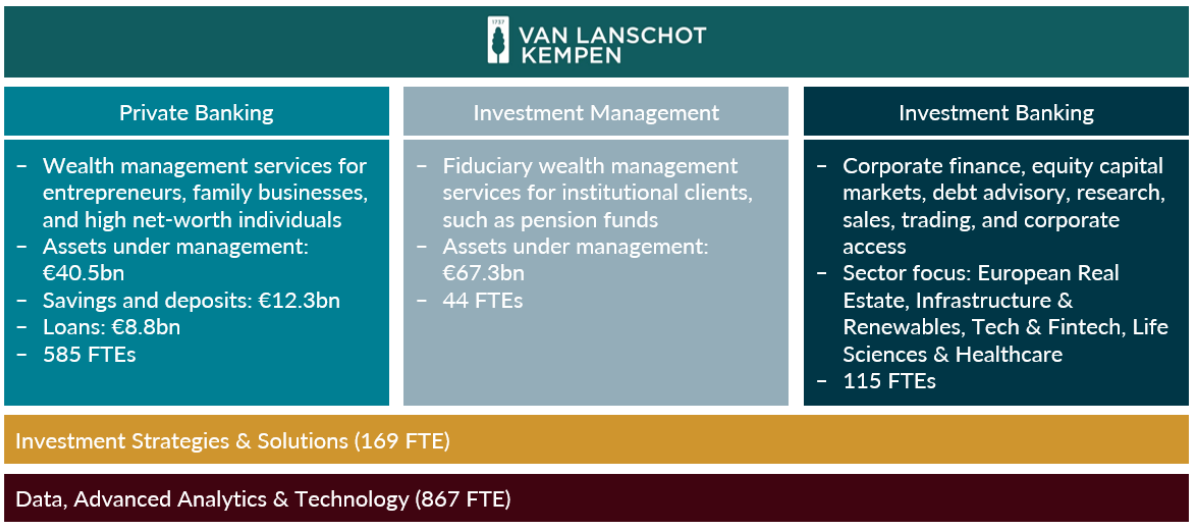

Figure 1 | Overview of Van Lanschot Kempen's organizational structure (adapted from Van Lanschot Kempen, 2023).

4. Dealmaking in life sciences and healthcare

To understand the relevance of CVRs in life sciences and healthcare M&A, it is essential to start by gaining insights into the industry's dynamics and the current market environment. In this chapter, we will explore the defining characteristics of the life sciences and healthcare sector, analyze the role of M&A, and look into the current trends influencing M&A in this industry. By doing so, we intend to lay the groundwork for understanding the broader context in which CVRs are employed and the factors contributing to the apparent upward trend in their use.

4.1 Introduction to the industry

The global life sciences and healthcare industry constitutes a dynamic sector that plays a vital role in advancing medical knowledge and therapeutic interventions. Within the healthcare domain, four subsectors can be identified, namely hospitals and health systems, physician practices, home healthcare and hospice, and healthcare IT (KPMG, 2023). These subsectors collectively provide comprehensive and patient-centric healthcare services. Within the life sciences domain, the industry can be subdivided into four additional subsectors, namely biopharma, diagnostics, medical devices (medtech), and biopharma services (such as contract research organizations (CROs) and contract manufacturing and development organizations (CDMOs)) (KPMG, 2023). Together, these actors are instrumental in driving innovation in drug development, diagnostics technologies, and medical devices, ultimately aiming to address unmet medical needs and improve overall healthcare outcomes. Van Lanschot Kempen predominantly focuses its efforts on the life sciences domain, which is why the scope of this report will be centered around this part of the industry with a main focus on the biopharma companies.

Biopharma companies are renowned for their significant investments in research and development (R&D), which is essential to improve existing therapies and to bring new therapeutic interventions to the market. The process of researching, testing, and bringing a new drug or medical device to market is time-consuming, risk-bearing, and capital-intensive. According to the European Federation of Pharmaceutical Industries and Associations (EFPIA), it takes an average 12-13 years before a new compound reaches the market and only one to two of every 10,000 newly synthesized compounds will succeed from drug discovery all the way through the Phase III trials (EFPIA, 2023). According to estimates of several research groups, the probability of obtaining U.S. Food and Drug Administration (FDA) approval for drugs entering a Phase I trial is approximately 3-30%, depending on the therapeutic indication and the method of calculation (Hay, Thomas, Craighead, Economides, & Rosenthal, 2014; Lo & Thakor, 2023; Wong, Siah & Lo, 2019). Moreover, the development of a new compound is incredibly capital-intensive with nearly 70% of the costs being incurred before the therapeutic intervention reaches the market to start generating revenues (EFPIA, 2023). The EFPIA reported that, in 2021, Europe and the United States spend approximately €42.5bn and €69.7bn on pharmaceutical R&D, respectively. Approximately 15% of these R&D costs were allocated to the preclinical phase, 49% to the clinical trials, with Phase III trials undoubtedly being the most costly, and the remaining 36% to regulatory approval, pharmacovigilance, and other matters (EFPIA, 2023).

Despite low probability of success and high costs, drug development remains a worthwhile endeavor due to the substantial earnings protected by patents and other forms of intellectual property protection (Lo & Thakor, 2023). Companies rely heavily on these patents to safeguard their discoveries and innovations, enabling them to generate revenues, recoup their R&D investments, and maintain a competitive advantage. Remarkably, by the end of 2030, the pharmaceutical industry is facing a so-called ‘patent cliff’ (Parrish, 2023). The ‘patent cliff’ is a term used in the pharmaceutical industry to describe a period during which multiple high-revenue-generating patents for brand-name drugs expire, leading to a significant decline in a pharmaceutical company's revenue. This phenomenon occurs because, once a drug's patent expires, generic versions can enter the market, offering the same therapeutic benefits at a fraction

of the cost. This influx of cheaper generic alternatives can lead to a sharp drop in sales and market share for the brand-name drug. It is estimated that between 2023 and 2030, 190 drugs will lose patent exclusivity and approximately $236bn in pharma sales will be at risk (Parrish, 2023). For pharmaceutical companies, the patent cliff represents a substantial financial challenge, as they must find new sources of revenue, e.g. developing and launching new drugs or expanding into other therapeutic areas, to compensate for the loss of exclusivity on their existing blockbuster drugs.

Within the Biopharma domain, various categories of organizations contribute to the development of the global R&D pipeline (IQVIA, 2023). According to IQVIA, the biopharma sector can be subdivided into academia, emerging biopharma companies, small, mid, and large pharmaceutical companies (IQVIA, 2023). While academia contribute less than 1% to the clinical R&D pipeline (Phase I-III), they play an important role in the preclinical development of drugs. The number of emerging biopharma companies – those with less than $500m in annual sales and less than $200m annual R&D spending – has increased with 26% since 2017. In 2002, these emerging biopharma companies were responsible for only a third of the global R&D innovation, as measured by their share in the Phase I to regulatory submission pipeline. In 2022, they were responsible for two thirds of the global R&D pipeline, indicating that smaller companies are becoming increasingly important for innovation. Intriguingly, the number of large pharmaceutical companies – those with more than $10bn annual sales – has remained stable since 2017, but they represent an increasingly smaller share of the clinical R&D pipeline (IQVIA, 2023). These observations raise the following two questions: 1) How do smaller biopharma companies with little or no revenue fund their R&D investments? 2) How do large pharmaceutical companies facing a 'patent cliff' maintain their competitive advantage? Together, the answers to these questions drive the underlying dynamics of dealmaking in the life sciences industry.

4.2 Industry dynamics

Funding of R&D investments

The dynamics of the life sciences industry are to a certain extent influenced by the funding strategies employed by emerging biopharma companies to support their R&D initiatives. Generally speaking, biopharma companies rely heavily on equity financing, especially the companies that do not have a positive cashflow yet (Lo & Thakor, 2023). Equity financing involves raising capital by selling company shares to investors in exchange for cash. Debt financing, on the other hand, is often not an attractive financing option due to the negative cashflow and limited tangible assets of biopharma companies (Lo & Thakor, 2023). Several forms of equity financing may be available to a biopharma company during its lifetime.

Consider, for example, an emerging biopharma company with no sales and substantial capital needed for R&D activities. During the early stages of drug development, such as preclinical research and Phase I trials, emerging biopharma companies typically seek funding from angel investors and venture capitalists (see Figure 2). These early investors provide critical capital to support initial research and proof-of-concept studies. As the drug development progresses to Phase II and III clinical trials, which involve larger-scale studies to assess safety and efficacy, larger investors, such as (corporate) venture capital firms and private equity, may come into play. These investors provide more substantial funding to support the extensive clinical testing required during these phases. Once a drug successfully completes Phase III and demonstrates its potential for market approval, the company may pursue a liquidity event to provide an exit for early investors and access additional capital for commercialization and further investments. This liquidity event can take the form of an IPO, where the company issues shares to the public, or an acquisition by a larger pharmaceutical company. It is important to emphasize that this is just one example, and in reality, biopharma companies might follow entirely different paths. For instance,

many pre-clinical and early-stage biopharma companies have successfully tapped into public equity markets through IPOs during the early stages of the COVID-19 pandemic (Lo & Thakor, 2023).

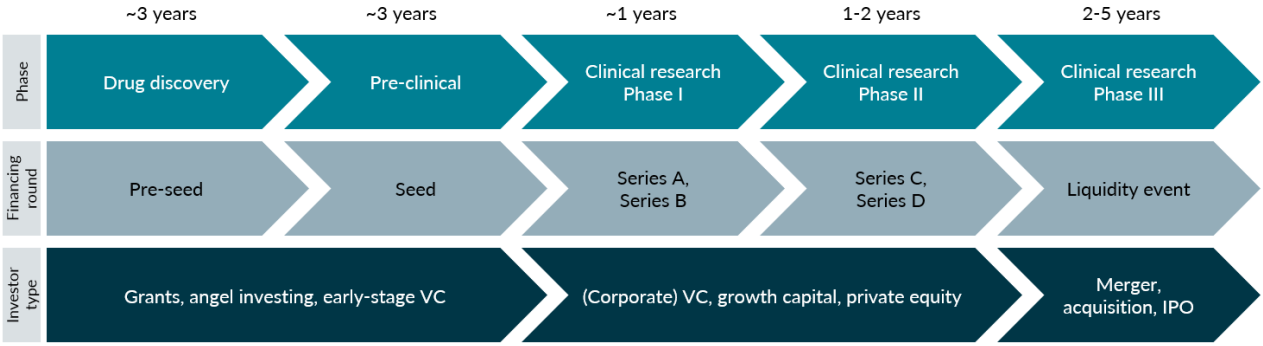

Figure 2 | An example of the different types of financing that may be available to a biopharma company with a successful product. *VC: Venture Capital; IPO: Initial Public Offering. Illustrative.*

The decision to pursue an IPO hinges on both internal factors, e.g. the strength of the R&D pipeline, management, and financial health, and external factors, e.g. market conditions and investor demand (Lo & Thakor, 2023). Exceptional valuations and bid premiums, notable investor interest, and high capital liquidity, allowed many emerging biopharma companies to enter the public markets via an IPO or a special purpose acquisition company (SPAC), ultimately resulting in a record of over 100 public listings in 2021 (Ernst & Young, 2023a). Following the heightened levels of funding during the COVID-19 pandemic, biopharma valuations dropped and IPOs, follow-on transactions, and venture capital investments slowed down in 2022 (see Figure 3) (IQVIA, 2023). The increasingly challenging conditions for IPOs are expected to make M&A exits and strategic partnerships a more appealing alternative in the second half of 2023 (Ernst & Young, 2023a). The shifting market conditions may enhance the attractiveness of M&A not only for emerging biopharma companies looking for an exit, but also for larger firms seeking to access so-called 'external innovation'.

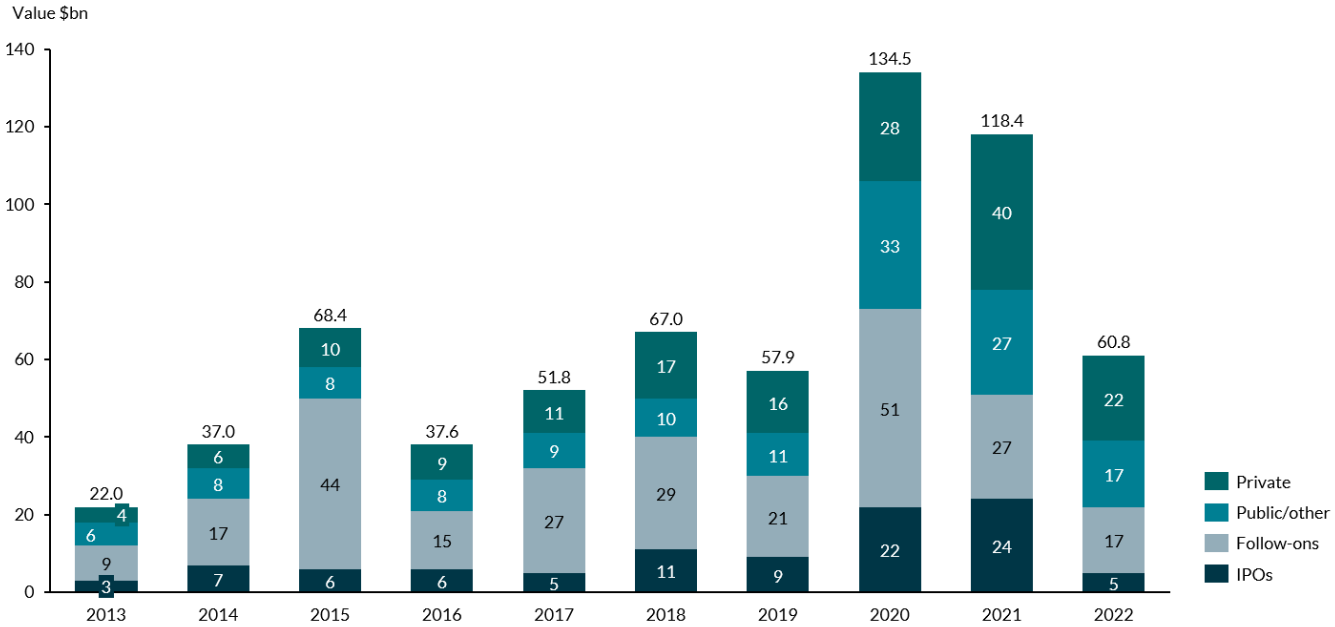

Figure 3 | Biopharma funding levels in the period between 2013-2022 (adapted from IQVIA, 2023). *Private: venture capital investments; Public/other: when public companies receive financing in some other way; Follow-ons: a public offering of shares that is not the IPO; IPO: Initial Public Offering.*

External innovation

While emerging biopharma companies with little or no revenues seek to obtain sufficient funding, large biopharma companies with established product portfolios strive to sustain long-term growth and competitiveness (Ernst & Young, 2020). As described before, large biopharma companies continuously need to invest in innovation in order to stay ahead of the patent cliff. These companies typically have a sizeable portfolio of approved products, that are already on the market and generating income. By using profits from current product sales to finance new R&D projects, these companies can continually innovate and expand their product pipeline while building and renewing their capabilities (Labiotech, 2023). However, these companies recognize that relying solely on internal innovation may not be sufficient maintain their competitive advantage.

External innovation has become an integral part of the biopharma business model. Large biopharma companies actively act as strategic investors, executing the majority of the biopharma deals to gain access to innovative technologies and therapies (see Figure 4) (Ernst & Young, 2020; KPMG, 2023). Research shows that these acquired technologies and product candidates have been responsible for most of large biopharma's earnings since 2014 (Ernst & Young, 2020). This trend becomes particularly evident for novel therapeutic modalities, such as cell and gene therapies, where numerous large biopharma firms initially failed to seize the organic investment opportunities. Conversely, emerging biopharma companies demonstrate remarkable efficiency in bringing new therapies to market, consistently achieving lower per-drug expenditure compared to their larger peers. In light of these findings, it becomes clear that large biopharma companies should focus their internal investments primarily on areas where they can maintain a competitive advantage, while simultaneously increasing their investments in external innovation (Ernst & Young, 2020).

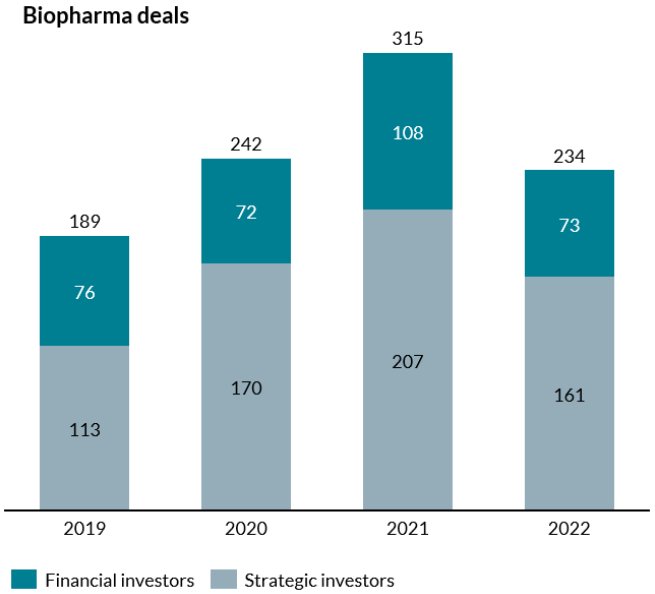

Figure 4 | Overview of biopharma M&A, indicating that a large share of the biopharma deals are done by strategic investors (adapted from KPMG, 2023).

An alternative option for obtaining external innovation is through strategic partnerships. Partnerships can be valuable for both companies involved, as it provides an opportunity for an emerging biopharma company to fund their R&D investments and for a larger biopharma company to obtain external innovation. From a smaller biopharma perspective, companies often seek strategic partnerships, including licensing and development deals, to pool resources, share

risks, and accelerate the pace of innovation (see Chapter 5.1). Large Biopharma companies with established market presence and resources may partner with smaller biopharma firms to gain access to their strategic resources, including their intellectual property, talent, and facilities (Ernst & Young, 2023a). Throughout the past years, strategic partnerships have become an increasingly important part of biopharma's M&A strategies (Ernst & Young, 2023a; Mergermarket, 2022). However, when companies seek rapid market entry and substantial growth within a short time period, M&A remains the strategy of choice (Mergermarket, 2022).

Taken together, MA& plays a fundamental role in the biopharma industry. For emerging biopharma firms, M&A serves as a critical liquidity event, providing early investors with an exit, and an opportunity to access additional resources. On the other hand, for larger biopharma players, M&A is essential to obtain external innovation and to maintain their competitive advantage. Moreover, it is anticipated that the challenging conditions for IPOs will make M&A exits more attractive in the second half of 2023 (Ernst & Young, 2023a). The following section will explore how the M&A industry evolved in recent years, and will examine the trends that are currently shaping M&A activity in the life sciences sector.

4.3 Biopharma M&A

The global M&A industry experienced a turbulent three years following the start of the COVID-19 pandemic. Transaction value rose to an all-time high of $1.5tn in the post-pandemic second quarter of 2021, and shrank to a mere $646bn in the first quarter of 2023 (Mergermarket, 2023). More specifically, the life sciences M&A industry experienced a substantial downturn in 2022. During that year, the sector recorded a mere $105bn in deals, marking a steep 53% decline from the previous year and representing the lowest transaction value since 2014 (Ernst & Young, 2023a). This downturn continued into 2023, as demonstrated by the numbers for Q1. In this quarter, only 269 life sciences deals were completed, a considerable decrease from the 438 deals executed in Q1 2022 (Calcagnini, 2023). The total transaction value for Q1 2023 equaled $69bn, skewed by the $43bn mega merger of Seagen and Pfizer, compared to $38bn total transaction value in Q1 2022 (Calcagnini, 2023). With biopharma M&A showing signs of stagnation, it calls for an in-depth analysis of the macro-environmental trends that are influencing the current M&A industry (see Figure 5).

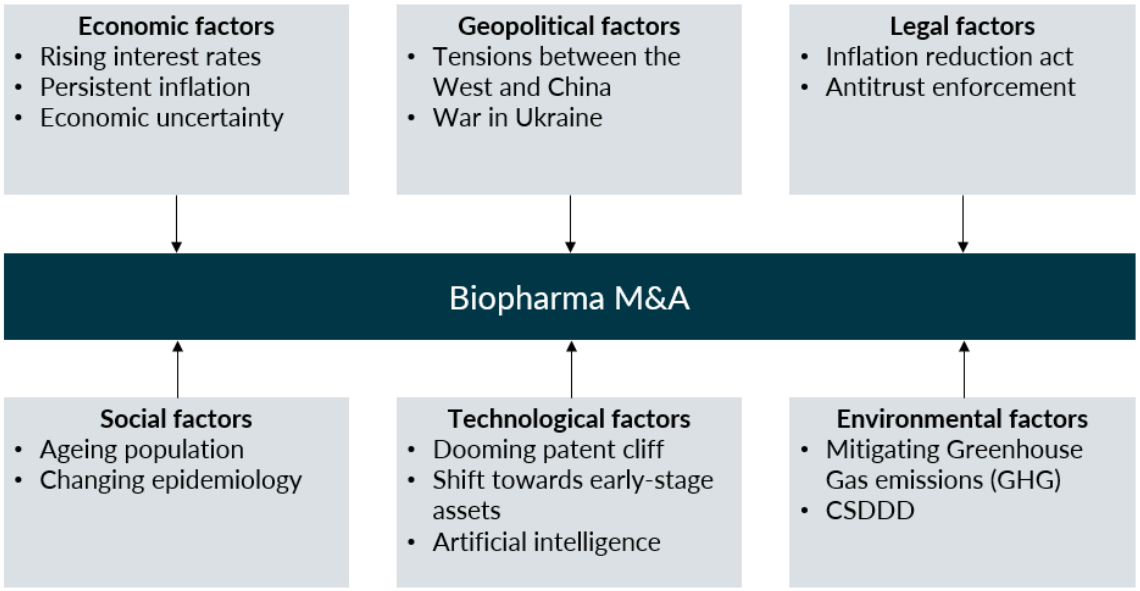

Figure 5 | Overview of macro-environmental factors shaping the biopharma M&A industry. *CSDDD: Corporate Sustainability Due Diligence Directive.*

From a macroeconomic and geopolitical perspective, the prevailing market conditions are negatively affecting biopharma's deal appetite and giving rise to a so-called buyer's market, i.e. a market where buyers have strong negotiation positions to secure favorable terms (Ernst & Young, 2023a).

Although the current economic challenges, i.e. rising interest rates, persistent inflation, and economic uncertainty, and geopolitical events, i.e. tensions between the West and China, and the war in Ukraine, had minimal impact on the business activities in the life sciences industry, it negatively affected biopharma M&A. Remarkably, the life sciences industry appears to be somewhat insulated from macroeconomic conditions (Mergermarket, 2023; Ural & Kumar, 2022). Historical data shows that the life sciences industry demonstrates considerable resilience during economic downturns, reflected by consistency in both dispensed prescriptions and R&D spending over the past 20-30 years (Ural & Kumar, 2022). While the geopolitical tensions did put pressure on global pharmaceutical supply chains, pharmaceutical demand or strategies were not negatively affected by the current market conditions (Ernst & Young, 2023b; Young, 2023). Conversely, in terms of M&A, the macroeconomic and geopolitical uncertainties of the past year have caused a significant downturn, as demonstrated by the low deal volumes and transaction values (Calcagnini, 2023; Ernst & Young, 2023a). The rising interest rates and the subsequent increase in the cost of capital, have put pressure on investor returns, thereby complicating the financing of M&A transactions. As a result, biopharma valuations dropped and investors' deal appetite remained limited in the last 12 months (Ernst & Young, 2023a; Ural & Kumar, 2022).

Yet, multiple emerging biopharma companies may experience growing pressure to sell themselves from the second half of 2023 onwards (Ernst & Young, 2023a). Smaller biopharma companies are approaching the end of their cash runways and are in need of financing. Although financial data on private biopharma companies is rather limited, it is worth noting that, as of March 31, 2023, 83 public biopharma companies had less than a year of cash and 217 of them were trading below cash (US) (William Blair, 2023). These numbers indicate that these companies will soon have to raise capital or pursue an exit strategy. Given that investor interest has cooled down and the route to the public equity markets has become more complicated (see Chapter 4.2), smaller biopharma companies might be inclined to resort to an M&A exit (Ernst & Young, 2023a). On the other hand, following record-high valuations in 2020-2021, the drop in valuations may provide an incentive for large biopharma companies to pursue an aggressive M&A strategy in second half of 2023 (Ernst & Young, 2023a).

From a regulatory perspective, there are two main factors shaping the biopharma M&A industry. The first major change in the legal environment of biopharma companies is the introduction of the Inflation Reduction Act (IRA). On August 16, 2022, the US government passed the IRA, which became active in January, 2023 (Golden et al., 2023). The IRA allows the Centers for Medicare & Medicaid Services (CMS) to negotiate purchases price of certain high-cost drugs (Golden et al., 2023). Although the law permits the CMS to negotiate prices for only a select group of drugs, it will have significant implications (Deloitte, 2023). As a result of the IRA, biopharma companies have been lowering the forecasts and valuations of affected drug candidates (KPMG, 2023). In the short term, the IRA is not expected to slow down dealmaking. However, it is worth noting that the law grants CMS the authority to negotiate prices for 10 drugs by 2026, and it may affect up to 60 therapies in 2030 (Bain & Company, 2023; KPMG, 2023). While this law is likely to put pressure on the valuations of certain high-cost product candidates, which will affect decision-making, the US remains the largest and most important sales market.

Second, the biopharma M&A industry will remain under close inspection from the Federal Trade Commission (FTC) in terms of antitrust enforcement (Golden & Hanks, 2023). In March 2021, the FTC and the US Department of Justice, together with state attorneys and regulators in Canada, the European Union, and the United Kingdom, decided to launch the Multilateral Pharmaceutical

Merger Task Force, which evaluates the way regulators measure the impact of mergers (Ernst & Young, 2023a). The FTC's firm conviction to prevent antitrust violations was demonstrated by the lawsuit filed against the $28bn acquisition of Horizon by Amgen, announced in December 2022. This acquisition would, allegedly, allow the combined entity to secure monopoly positions in certain therapeutic indications (Cision PR Newswire, 2022; Liu, 2023a). The antitrust enforcement by the FTC may cause large biopharma companies to move away from certain acquisitions.

Sociological factors may play a role in shaping M&A activity within the life sciences and healthcare sector, although their impact is probably less pronounced compared to other factors (KPMG, 2023). The ageing population represents a significant demographic shift, leading to an increase in healthcare demand and a higher prevalence of chronic diseases and comorbidities (Atella et al., 2019; KPMG, 2023). Additionally, there is a growing number of people suffering from obesity and diabetes (Mobasseri, 2020). Changes in demographics and epidemiology may encourage biopharma companies to steer their investments towards certain therapeutic indications. To illustrate, in response to the COVID-19 pandemic, numerous biopharma companies swiftly made the decision to enter the market for vaccines and other COVID-19-related treatments (McKinsey & Company, 2020). It is important to note that the changing demographics and epidemiology are indeed driving changes, but these effects may take time to significantly reshape the biopharma M&A landscape.

Not unexpectedly, technological factors play a major role in the biopharma industry. As described before, an important driver for M&A in the life sciences sectors is the fact that large biopharma companies are facing a patent cliff (Ernst & Young, 2023a; Parrish, 2023). It is estimated that between now and 2030, more than $230bn in pharma revenues is at risk as a result of 190 drugs losing patent protection (KPMG, 2023). Large biopharma companies must invest heavily in both their internal innovation, through R&D spending, and external innovation, via M&A and strategic partnerships, to maintain their competitive edge and sustain their long-term growth (Ernst & Young, 2023a; KPMG, 2023). Remarkably, as of 2022, biopharma companies had more than $1.4tn available to fund strategic initiatives, which is an +11% increase compared to 2021 (Ernst & Young, 2023a). Moreover, at the beginning of 2023, the top 25 life sciences firms held a combined $130bn in cash on their balance sheets (Bain & Company, 2023; Ernst & Young, 2023a). These numbers indicate that large biopharma companies have sufficient capital available to invest in technologies and drug candidates that will offset the upcoming losses through strategic dealmaking in the coming year.

More specifically, in the past years, biopharma M&A has shifted from late-stage/marketed assets to early-/mid-stage assets (see Figure 6) (Ernst & Young, 2023a). For a long time, biopharma companies aimed to acquire relatively de-risked Phase III/marketed assets. However, in 2022, a mere 5% of the total deal volume could be attributed to deals involving a Phase III asset, in contrast to the 13.0% observed in 2021. This indicates that biopharma companies have realized that acquiring relatively de-risked assets requires paying a significant premium (Ernst & Young, 2023a). This shift away from late-stage/marketed assets suggests that the competition for the acquisition of a limited number of innovative, early-stage targets will intensify (KPMG, 2023).

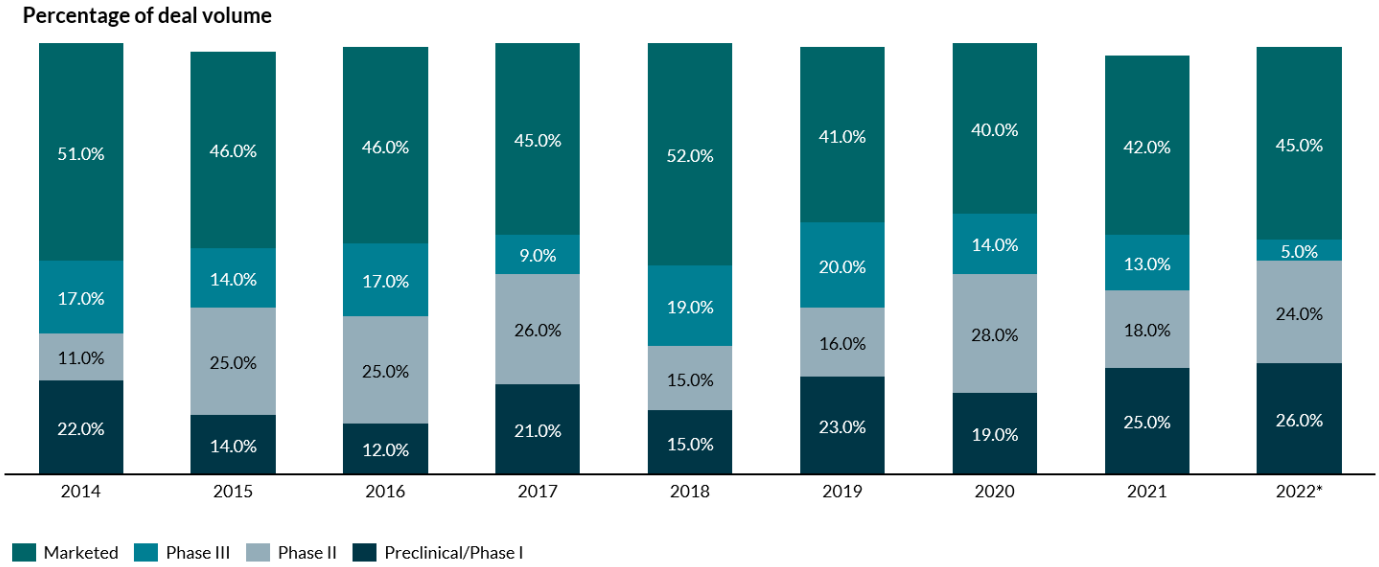

Figure 6 | Overview of the percentage of deals based on the development phase of the most advanced asset, indicating a shift from late-stage/marketed asset to early-/mid-stage assets (adapted from Ernst & Young, 2023a). *Percentage may not add up to 100 due to rounding.*

Additional technological developments worth noting are the breakthroughs in technologies in different fields, such as artificial intelligence (AI), quantum computing, big data, and robotics, which could have large impacts on the life sciences industry (Ernst & Young, 2023a). For example, life sciences companies may be able to use AI to transform the drug discovery process, reducing the time required for screening to preclinical testing, thereby lowering the costs for the identification of potential new drug candidates (Deloitte, 2023). Increasingly, biopharma companies will shift their investments to digital technologies and data science (Ernst & Young, 2023a).

Lastly, evolving ESG and climate change regulations are expected to have a serious impact on M&A activity in Europe (Mergermarket, 2023). The EFPIA, comprising 37 national associations, 38 leading pharmaceutical companies, and a growing number of small and medium-sized enterprises, is already actively engaged in combating global warming by mitigating greenhouse gas (GHG) emissions (EFPIA, 2020). EFPIA members are tackling climate change by implementing strategies to reduce CO_2 emissions, adopting alternative energy sources, fostering the development of sustainable products and eco-friendly packaging, and actively working to reduce scope 3 emissions, i.e. emissions throughout the entire value chain (EFPIA, 2020). However, biopharma companies will need to intensify their efforts even further. On June 1, 2023, the European Parliament published a statement regarding its position on the Corporate Sustainability Due Diligence Directive (CSDDD) (Bosselaar, Bloemen & Pennink, 2023). The CSDDD is a regulatory initiative that will require companies of a certain size to carry out due diligence on, and take responsibility for, human rights violations and environmental damage across their global value chains (Bosselaar et al., 2023). Although the CSDDD will probably not be formally adopted before 2024, it is expected to significantly affect the life sciences and healthcare industry (Mergermarket, 2023). These new regulations will presumably motivate biopharma companies to investigate the ESG implications of every M&A target they consider (Mergermarket, 2023).

To sum it up, the biopharma M&A industry faced significant challenges in 2022 and 2023. The analysis of the macro-environmental factors revealed both negative and positive drivers for biopharma M&A. On the one hand, the industry suffered from higher cost of capital, falling valuations, and diminished investor interest. On the other hand, M&A activity may be positively influenced by the closed IPO window, limited cash runways of emerging biopharma companies,

and the approaching patent cliff and substantial cash reserves of large biopharma companies. Looking ahead, several factors influencing biopharma M&A activity in the long term have been identified, including antitrust regulations, emerging technologies, and evolving ESG regulations.

4.4 Insights & reflections

This chapter offers valuable insights into the dynamics and trends influencing the biopharma M&A industry. M&A serves as an important tool, providing emerging biopharma firms exit opportunities and providing large biopharma companies with access to external innovation. While the past year saw a notable decline in biopharma M&A, there are promising signs indicating that dealmaking activity might take off in the second half of 2023.

In the past year, the prevailing market conditions gave rise to a buyer's market and a corresponding drop in biopharma valuations. This decline in valuations has likely led to substantial gaps between what sellers expect their assets or companies to be worth and what buyers are actually willing to pay. These differences in pricing expectations make it even more difficult for M&A transactions to materialize. It is anticipated that, from 2023 onwards, there will be an increase in the number of deals involving creative equity financing, milestone-based agreements, or CVRs, to bridge the valuation gaps that have emerged (Filippi & Franklin, 2023; Golden & Hanks, 2023; KPMG, 2023).

5. Contingent value rights in biopharma M&A

While it is widely acknowledged that CVRs are used to 'bridge a valuation gap', this chapter takes a closer look to determine whether that is indeed their sole use case. We will investigate the different types of CVRs, discuss their pros and cons, examine how frequently they are used, and assess the apparent upward trend in their use. Furthermore, we will shed light on the relatively limited use of CVRs in Europe, and explore the barriers hindering their application in this area, using insights from legal and financial experts. However, before we delve into the intricacies of CVRs in biopharma M&A, it is essential to gain a better understanding of how biopharma companies are valued and why this is often not as straightforward as one would hope.

5.1 Valuation of biopharma companies

Valuation methods

When two companies decide to examine the possibility of an M&A transaction, the valuation of the target company becomes a critical element. Commonly used valuation methods are comparable company analysis (CCA), comparable transaction analysis (CTA), and discounted cash flow (DCF) analysis (Rosenbaum & Pearl, 2020). CCA and CTA are based on the premise that similar public companies or M&A transactions can be used as a benchmark for the valuation of the target company. These comparables companies or transactions are selected based on shared characteristics, such as business profile (e.g. sector, product/service, customers, distribution channels, geography), financial metrics (e.g. size, profitability, growth), and risks. In both CCA and CTA, the valuation process primarily relies on multiples, such as Enterprise Value to Earnings Before Interest, Taxes, Depreciation, and Amortization (EV/EBITDA) and Price-to-Earnings (P/E) ratios. These multiples offer a quantitative perspective on a company's value relative to its earnings or other financial metrics (Rosenbaum & Pearl, 2020). However, while CCA and CTA prove effective in many industries, they often encounter limitations for the valuation of biopharma companies (Rottgen, n.d.). Biopharma companies, known for their innovative technologies, are often unique, making it challenging to compare them to others in the industry. Moreover, as described in Chapter 4, a large part of the biopharma companies operates without generating revenues, let alone profits, which makes conventional valuation multiples like EV/EBITDA or P/E ratios less applicable (Rottgen, n.d.).

The third commonly used valuation method is a DCF analysis, which is a fundamental valuation method based on the premise that the value of a company can be derived from the present value of its anticipated free cash flows (FCFs) (Rosenbaum & Pearl, 2020). FCFs represent the surplus in cash generated by a company's operations after deducting expenses, investments, and debt repayments, providing an indication of a company's capacity to distribute capital to shareholders or repay debt. A company's future FCFs may, for example, be projected by extrapolating historical numbers and trends. However, given that many biopharma companies do not generate revenues yet, it is often impossible to project historical FCFs into the future. Even in the case of larger biopharma companies that do generate sales, simply extrapolating historical data is often not suitable due to the idiosyncratic nature of drug sales (Rottgen, n.d.). Therefore, valuing a biopharma company using a DCF analysis requires gaining a deep understanding of the company's business model, making informed estimates the size and duration of future FCFs, and assigning probabilities of success to clinical trial outcomes and regulatory approvals.

Biopharma business models

The first step in valuing a biopharma company is comprehending the details of its business model, which provides insights into the potential revenue streams and subsequent future FCFs. Broadly

speaking, three types of business models can be employed by biopharma companies, namely technology partnering, asset creation and out-licensing, and product development and commercialization (see Figure 7) (Labiotech, 2023). In practice, companies often employ a combination of these three business models.

The technology partnering business model often involves emerging biopharma companies owning valuable technological intellectual property, which they can license to other, often larger players in the life sciences sector. This approach allows these companies to generate revenue by collaborating with better-funded counterparts. Under this model, the company assuming the role of the partner takes on most of the risks, but it also holds all the potential upside. Revenues generated in such partnerships typically include upfront payments, fee-for-service payments, and preclinical milestone payments. In return for these payments, the partner holds all the rights to any pharmaceutical asset resulting from the partnership.

In the asset creation and out-licensing business model, a company invests its capital in developing (pre-)clinical assets, which can then be exclusively licensed to larger biopharma companies. In this partnership, the partner takes on the responsibility of funding the often costly late-stage clinical trials, navigating the regulatory approval processes, and handling marketing efforts. Licensing agreements typically include an upfront payment, milestone payments, and royalties based on future product sales. This model taps into the partner's expertise in late-stage development and commercialization. Conversely, for the larger biopharma company, licensing partnerships provide quick access to external innovation, moderate costs, and control over the late-stage development. An illustrative example of a company using the technology partnering business model is Sigilon Therapeutics – the company discussed in the case study in Chapter 6.

Lastly, biopharma companies may opt for a product development and commercialization model. Under this business model, the company develops a pharmaceutical asset independently, thereby maintaining full ownership. This business model typically demands significant financial resources and/or an existing revenue streams from a portfolio of assets. It comes with higher risks as it involves expertise in development, manufacturing, regulatory approvals, payer reimbursement negotiations, and commercialization. Even larger biopharma companies utilizing this model may lack expertise in some of these areas and bridge these gaps through strategic partnerships (Labiotech, 2023). Moreover, as described in Chapter 4, large biopharma companies may take part in strategic partnerships or pursue an M&A strategy to obtain access to external innovation (Ernst & Young, 2020). An example of a company leveraging this approach is Eli Lilly – the other company discussed in the case study in Chapter 6.

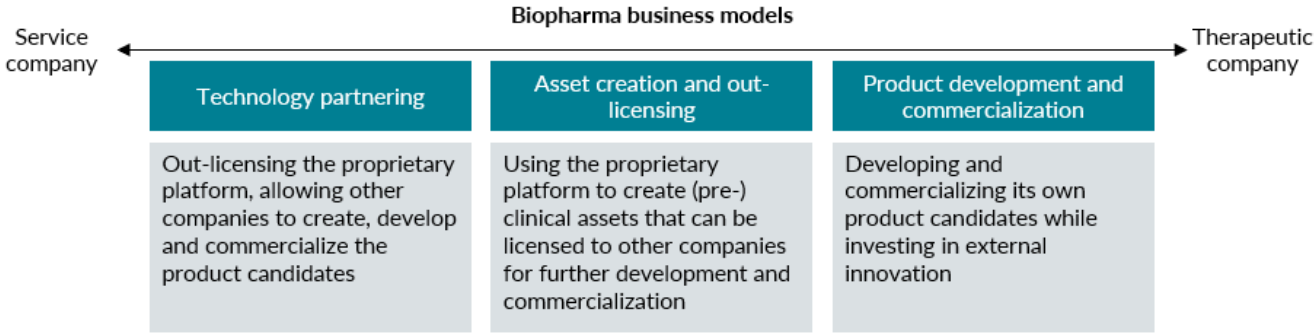

Figure 7 | Simplified overview of biopharma business models (adapted from Deloitte, n.d.). In practice, biopharma companies often use a combination of these business models.

Estimating future free cash flow

Once the main drivers of the business model have been characterized, it is possible to estimate future cash flows for each asset. The following section serves as a simplified overview of the process for estimating FCFs of a biopharma company developing one pre-clinical asset using their proprietary technology.

An important step involves estimating the cash outflows associated with the development of that asset. R&D costs, which are incurred in the absence of revenues, depend on numerous factors, including the type of technology, the development phase, the number of patients required for clinical trials, the therapeutic indication, etc. Apart from R&D costs, cash outflows associated with regulatory approval and commercialization must be covered. Moreover, estimates should be made with regards to how efficient the company is developing and/or selling their products, involving an estimation of their selling, general & administrative (SG&A) expenses, working capital, depreciation and amortization, and capital expenditures (Rottgen, n.d.).

After obtaining regulatory approval, the asset is expected to generate revenues and profits. A main driver of biopharma revenues is the size of the attainable market, which is influenced by the number of patients and the price of the therapeutic intervention (Deloitte, n.d.). The number of patients depends, for example, on the prevalence of the therapeutic indication, the eligibility criteria for patients (such as 1st/2nd/3rd line therapy, disease subtypes, patient fitness, and geographic reach), and the estimated market share (dependent on standard of care, alternative treatments, and marketing efforts) (Deloitte, n.d.; Rottgen, n.d.). On the other hand, drug pricing is shaped by a complex interplay of factors, including, but not limited to, return on R&D investment, alternative treatment options, and often undisclosed negotiations. Furthermore, the time until a patent expires plays a crucial role in determining future cash flows, as it leads to generic competition and a subsequent drop in sales (Deloitte, n.d.).

After estimating the future FCFs, they should be discounted to the present value, using a discount factor. This calculation will yield the standalone enterprise value of the company while taking into account the time value of money (Rosenbaum & Pearl, 2020; Rottgen, n.d.). For the valuation of a biopharma company, it is important to recognize that certain risks can have significant influences on the final valuation. These risks include, for example, clinical trial outcomes or regulatory approvals. To provide a more 'fair' valuation of the company, probabilities of success can be assigned to each phase of drug development, using historical data (Hay et al., 2014). By incorporating these probabilities, a risk-adjusted enterprise value can be derived. This approach provides a more conservative estimate of a biopharma company's value, reflecting the uncertainties inherently related to drug development (Rottgen, n.d.).

To conclude, the biopharma industry distinguishes itself from traditional sectors through its unique business models and value creation methods. Unlike traditional sectors that may focus on operational improvements, biopharma companies create value by developing pioneering technologies and product candidates. Valuing a biopharma company involves assigning probabilities of success to critical milestones in the company's drug development process. These milestones, such as obtaining regulatory approval for a new drug, are binary events. As a result, in this industry, companies either succeed or fail, leading to more volatility but also the possibility of greater returns.

5.2 Contingent value rights

Bridging valuation gaps

Of all the issues that may arise during an M&A transaction, the most crucial one is valuation. It is not uncommon for an acquirer and a target company to have different valuations in mind. Sellers may still hold on to higher valuation expectations, while buyers are inclined to negotiate for lower prices. As described in Chapter 4, biopharma valuations have experienced a decline in the past year, contributing to the emergence of a buyers' market (Ernst & Young, 2023a). As a result, acquirers may take a more conservative approach, considering the uncertainties and risks associated with drug development, regulatory approvals, and competition. On the other hand, selling companies may have a more optimistic view of their assets, placing a higher value on their technology platform and product candidates (Rottgen, n.d.). When rigorous due diligence and extensive discussions do not successfully address this valuation gap, legal and financial dealmakers can try to facilitate the negotiations using a number of tools, including the CVR (Kirman et al., 2011). However, it is essential to note a CVR is not the only solution to address a valuation gap (Holthuis, 2016). If other methods can help two parties to reach an agreement, what sets CVRs apart, and under what circumstances do these instruments provide an added benefit?

Trends in the use of CVRs

CVRs emerged in the late 1980s as a contractual agreement in which the buying party commits to paying additional consideration to the selling party when specific payment triggers are met, within a specified period of time (Kirman et al., 2011). Generally speaking, two main types of CVRs exist, namely price-protection CVRs and event-driven CVRs. Price-protection CVRs are designed to provide the selling party with downside protection against a potential decrease in the value of a stock consideration in a public company acquisition. Conversely, event-driven CVRs can be used in public takeovers to provide additional value to the selling shareholders based on the achievement of specific milestones after the transaction's closing within a specified period of time. While historically, price-protection CVRS were more commonly used, over time, event-driven CVRs have become increasingly popular (Kirman et al., 2011). Of note, since 2018, there has been only one publicly disclosed M&A transaction that featured a conventional price-protection CVR, and it was not for the acquisition of a biopharma company (Wagner Partin et al., 2023). Interestingly, several sources suggest that the biopharma industry is experiencing a considerable increase in the number of CVRs (Golden & Hanks, 2023; KPMG, 2023; Miller, 2023; Wagner Partin et al., 2023).

In the United States, the year 2022 saw a growing number of CVRs compared to 2021, and the trend continued into 2023, with at least four public takeovers including a CVR in the first months alone (AstraZeneca, 2023; Becker, 2023; Ipsen, 2023; Satsuma Pharmaceuticals, 2023; Wagner Partin et al., 2023). From January 1, 2018, through April 30, 2023, out of a total of 1,119 public deals announced across all industries, only 37 (~3%) included CVRs (Wagner Partin et al., 2023). Remarkably, approximately 84% of these deals with CVR were in the life sciences industry, indicating that CVRs are especially suitable for this sector. Conversely, during the five-year period preceding that (January 2013 to December 2017), there were 25 public transactions that involved a CVR, accounting for approximately 2% of all announced deals. Among these 25 transactions, 72% were related to the life sciences sector (Wagner Partin et al., 2023).

These numbers indicate a statistically relevant increase in the overall number of deals incorporating a CVR (25/1,250 in Period 1 compared to 37/1,119 in Period 2), and in the number of biopharma deals involving a CVR (18/25 in Period 1 to 31/37 in Period 2). While these findings suggest a statistically significant increase between these two periods, the analysis does have limitations. The most recent period is four months longer and the dataset is rather small. If we exclude four life sciences deals from the analysis (those announced in the early months of 2023), the statistical difference becomes less pronounced. Nonetheless, the four biopharma deals

announced in the first few months of 2023, are already nearing the annual average of 5-6 CVRs across all industries. Thus, we can confidently state that CVRs are especially prevalent in the life sciences industry, and that their appeal has continued to grow in the past months.

The attractiveness of CVRs within the life sciences sector can be attributed to the fact that biopharma companies are particularly well-suited for this instrument. As described before, biopharma business models often revolve around strategic partnerships with larger biopharma companies. These licensing deals typically include upfront payments and (pre-)clinical milestone payments . Similarly, CVRs in life sciences transactions are typically event-driven, meaning that the payment is contingent on achieving specific milestones, such as clinical trial outcomes, regulatory approval of a drug or future peak sales (see Figure 8). Moreover, sellers life sciences industry are familiar with the earnout payment structure for private companies, making them more inclined to accept similar deal terms in the public company context (Kirman et al., 2011).

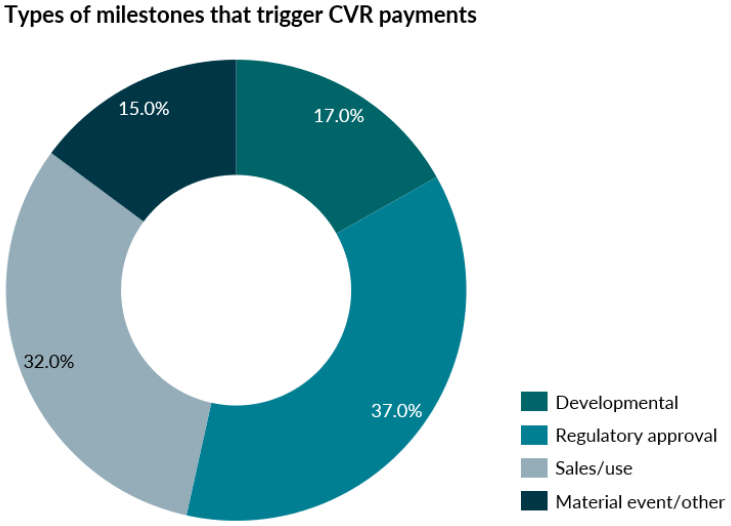

Figure 8 | Pie chart depicting the types of milestones that trigger event-driven CVR payments in life sciences deals during the period between January 2018 and April 2023 (adapted from Wagner Partin et al., 2023).

Generally speaking, CVRs in biopharma deals represent anywhere from 1% to 30% of the upfront deal value, are often designed to be paid out in cash rather than in stock (89%), and are largely non-transferable (92%) (Kirman et al., 2011; Wagner Partin et al., 2023). Transferable CVRs, on the other hand, are traded on stock exchanges, effectively making them securities that can be bought and sold by CVR holders. To achieve listing on a stock exchange, certain requirements set by the SEC must be met. For instance, in the case of the New York Stock Exchange, a CVR must have a minimum of 1 million CVRs outstanding, at least 400 holders, a lifespan of at least one year, and a minimum market value of $4 million (Kirman et al., 2011). Although it is not common practice, there are times when parties decide to list CVR, as illustrated by cases like the Sanofi-Aventis-Genzyme CVR and the Bristol-Myers Squibb-Celgene CVR (detailed below). Having covered the different types of CVRs and the frequency of their use, the next step is to investigate when these instruments prove to be particularly beneficial.

CVRs in practice

Generally speaking, CVRs can be used as a tool to align the interests of two parties in public M&A negotiations. The decision to incorporate a CVR into a deal structure can be influenced by several factors. However, it is essential to understand that the choice to utilize a CVR often emerges from a complex interplay among these factors, and there is no single, definitive scenario where a CVR proves useful.

For example, a CVR may become useful when there is asymmetric information on the attractiveness of (part of) the assets or when there are challenges in estimating the value of the company (Kirman et al., 2011). From the perspective of the selling shareholders, a CVR provides an opportunity to maintain a stake in the potential future success of a specific asset, allowing ongoing investment exposure to that asset, rather than to a broader portfolio, as would be the case with an equity payment. From the acquirer's perspective, a CVR offers a chance to share the risk of drug development or to persuade selling shareholders to close the deal. Moreover, in times of economic uncertainty, when the market shifts from a seller's market to a buyer's market, an increase in the number of CVRs can be expected, as they offer an attractive solution to address risks associated with the future performance of the company (Filippi & Franklin, 2023). Ultimately, the decision to include a CVR in the deal structure is shaped by a variety of factors that may not always be readily apparent. Therefore, these factors should be assessed on a case-by-case basis (see Chapter 6).

Although CVRs offer substantial advantages, they are not without their risk. One significant issue surrounding the use of CVRs is the complex process of its valuation. Determining the fair value of the CVR can be a complex task and may lead to disagreements between parties involved in the transaction (see Chapter 5.3). Furthermore, CVRs are predominantly employed in the United States and are less commonly used in European deals, indicating that there may be a geographical hurdle (see Chapter 5.3). Another notable drawback associated with CVRs is the risk of disputes and litigation (Filippi & Franklin, 2023; Wagner Partin et al., 2023). Given that the buyer is, in large part, in control of achieving the payment-triggering milestones, the seller will want to impose certain post-closing efforts on the buyer. In contrast, the buyer's objective is to ensure that these obligations are reasonable and that they will not necessitate ongoing investments if unexpected circumstances affect the project's profitability. To this end, contractual terms, such as the commonly used 'commercially reasonable efforts' and 'diligent efforts' clauses, are incorporated in the CVR agreement. However, these terms lack clear legal definitions, which leads to interpretation challenges (Filippi & Franklin, 2023; Wagner Partin et al., 2023). Several major lawsuits have been filed claiming that the buyer did not devote sufficient resources to achieve the milestones, allowing them to avoid milestone payments to the CVR holders.

To illustrate, in 2019, Bristol-Myers Squibb (NYSE: BMY) (BMS) announced that it would acquire Celgene Corporation (Nasdaq: CELG) in a cash and stock transaction valued at $74bn (Liu, 2023b). Celgene shareholders would receive 1.0 BMS share, $50.00 in cash, and one tradeable CVR for each share of Celgene. The CVR holders were entitled to receive a one-time payment of $9.00 in cash upon FDA approval of ozanimod by December 31, 2020, liso-cel by December 31, 2020, and bb2121 by March 31, 2021, in each case for a specified therapeutic indication (Liu, 2023b). Later, in June 2021, former Celgene shareholders claimed that BMS intentionally delayed FDA-approval of liso-cel to avoid the CVR payment of $6.4bn (Dunleavy, 2021). If liso-cel would get FDA-approval by the end of 2020, it would trigger a CVR milestone payment. However, due to alleged missteps by BMS and its manufacturing contractor Lonza, the drug gained approval from the FDA in February 2021, thereby avoiding the $6.4bn CVR payment to former Celgene shareholders. Eventually, the federal judge found no proof of BMS intentionally delaying the approval process (Liu, 2023b).

Another example of the litigation risk is the acquisition of Genzyme Corporation by Sanofi-Aventis. In 2010, Sanofi-Aventis launched a hostile takeover offer for Genzyme (Kollewe & Milmo, 2010). In 2011, Sanofi-Aventis reached an agreement to acquire Genzyme for $74.00 in cash and one CVR per share, bringing the total deal value to $20.1bn (FiercePharma, 2011). The CVR entitled the shareholders to receive additional cash payments if specified development milestones related to

Lemtrada™ or certain production volumes in 2011 for Cerezyme® and Fabrazyme® were achieved (FiercePharma, 2011). In 2015, former Genzyme shareholders sued Sanofi for purposely stalling Lemtrada™ development to avoid the milestone payment related to FDA approval (Sagonowsky, 2019). Former Genzyme shareholders claimed that the 8-month delay was intentional and prevented them from receiving a minimum of $708m CVR milestone payment. Ultimately, Sanofi-Avantis paid the shareholders $315m to settle the claim (Sagonowsky, 2019). These legal disputes over CVR payments emphasize the need for transparent agreements, compliance, and accurate records. While CVRs can be useful for aligning interests and mitigating risks, they should be carefully defined to avoid legal conflicts.

To summarize, CVRs serve as tools to address valuation gaps in public M&A deals, which may have arisen due to a variety of reasons, including asymmetric information, different perceptions on risk, and falling valuations. Notably, CVRs are commonly employed in the life sciences industry, and several sources substantiate their growing adoption in the United States in recent years. In contrast, to date, there have been few, if any, biopharma deals between two European companies that included a CVR.

5.3 Insights from industry experts

In order to gain a deeper understanding of the use of CVRs in European biopharma M&A, two professionals provide their perspectives. Drawing from more than ten years of experience in the field of public M&A, a lawyer sheds light on the regulatory aspects of CVRs in Europe. Complementing his perspective is a financial professional with over a decade of hands-on experience, who was involved in structuring a life sciences deal that included a CVR component.

Plan B solutions

Both professionals explain that a CVR can come into play when the buyer and the seller are highly motivated to close a deal, but they face a substantial valuation gap. The legal professional explains how CVRs can be employed by using Steinhoff International as an example. Steinhoff International, a large conglomerate with a Dutch holding, was recently facing difficulties due to a major fraud scandal. The company's valuation plummeted from €20bn to a mere fraction of that. Given that the company's assets were worth €3.5bn, while its debt stood at approximately €10bn, a comprehensive restructuring became inevitable. The banks were willing to extend the debt repayment, but only if they got full control over the company. This put existing shareholders in a tough spot, as their shares would become effectively worthless. Steinhoff's management recognized the need to offer the existing shareholders an alternative in order to 'sweeten the deal': the implementation of a CVR. This approach aimed to address the uncertainty surrounding the company's future valuation, allowing existing shareholders the potential to benefit if the company's assets were to recover in the coming years. The Steinhoff International deal was a significant moment in the legal professional's career, as this CVR was a first-of-its-kind within the Dutch jurisdiction.

The financial professional provides further insight into the applicability of CVRs in biopharma M&A. According to him, another circumstance where CVRs may prove useful is when the buyer is eager to proceed with the acquisition but wishes to share some of the inherent risks. For example, the buyer may hold a positive view of a drug but recognizes the potential risks associated with its Phase III trials. In this case, they may propose a payment structure where one part is paid upfront and the other part is paid upon successful completion of Phase III, thereby sharing the risk with the seller. However, it is essential to note that such arrangements might not always be favorable to

the seller. In some cases, sellers might have little choice but to accept CVRs, either because the overall deal is exceptionally attractive or due to a lack of alternative options.

CVRs in Europe

To date, CVRs have gained significant traction in the United States, especially in the healthcare sector, while their adoption in Europe has been relatively limited. Both professionals conclude that the limited use of CVRs in Europe can be predominantly attributed to the fact that they are not yet 'market practice'.

The M&A lawyer emphasizes that there are no barriers within the Dutch legal system that prevent the use of CVRs. He mentions that the concept of CVRs is relatively new in many European jurisdictions, creating a level of uncertainty and hesitancy among stakeholders, including dealmakers, shareholders, and regulatory authorities. Stakeholders often seek (legal) precedents to rely on. However, he states that a trend like this one, often starts in the United States, gradually extends to the United Kingdom and eventually, reaches the broader European market. Furthermore, American bidders are familiar with this instrument, so when they engage in acquisitions in Europe, they might choose to utilize it.

The financial professional expands on the reasons underlying the differences in the use of CVRs between the United States and Europe. Generally, people in the United States take a less conservative approach to dealmaking and are typically more inclined to explore creative solutions. The concept of CVRs has a longer history and is more commonly embraced in the United States compared to Europe. Regulatory authorities in Europe often grapple with the concept, which adds an extra layer of risk that transactions may not materialize. In contrast, the Securities and Exchange Commission is well-acquainted with CVRs and is more receptive to their usage. Lastly, it is important to note that, naturally, given the higher volume of deals in the United States, it follows that a greater number of deals feature CVRs compared to Europe.

Shifting market dynamics

Both professionals agree that market conditions indeed have a notable impact on the prevalence of CVRs in transactions. The legal professional underscores that uncertainties in the market, driven by factors like geopolitical events and rapid changes, make it challenging to precisely assess an firm's future value. The financial professional builds upon the discussion by explaining that, typically, CVRs serve as a tool to bridge valuation gaps between buyers seeking to maximize value creation and sellers aiming to secure higher returns. When the market is riding high and then takes a downturn, sellers may still hold onto the high valuations from a year ago, while buyers base their offers on the current lower market values. This disparity creates a gap that CVRs can effectively address. While the financial professional acknowledged that he had not conducted research on this topic, he hypothesized that during a market downturn, you are likely to witness a surge in the use of CVR agreements as a solution to the challenges posed by fluctuating market conditions.

Valuation

Valuation issues, rather than legal hurdles, often appear to be the main obstacle to the use of CVRs. The legal professional emphasizes that determining the exact value of a CVR is a concern shared across different countries and industries. In many cases, both buyers and sellers prefer to receive an upfront cash payment rather than a potential cash payment in the future. Therefore, CVRs are frequently used as negotiation tools, allowing parties to use them as part of the bargaining process when they are confident about the occurrence of specific future events. However, the legal professional concludes that, ultimately, the preference for most stakeholders, whether as sellers

or buyers, is to secure an upfront cash payment, making CVRs a secondary option, typically a Plan B, in transactions.

The financial professional agrees on the views of the legal professional when it comes to the valuation of a CVR. The true issue lies in the need to value a CVR, which inherently involves uncertain future events. Valuation requires financial advisors to make assumptions about the probability of these events occurring. The financial expert illustrates this challenge by considering an example of a CVR linked to the success of a Phase III clinical trial for an oncology product. Historical data might suggest, for example, a 60%, 70% or 80% chance of success, which leaves substantial room for discussions. The binary nature of the event complicates assigning a precise value even further. He notes that creating a listed CVR might be a solution as it allows the market to determine its value. Listed CVRs, such as the BMS-Celgene example, showcase that the market's estimation of the likelihood of success can reflect a more cautious and less optimistic view on the potential CVR payments.

5.4 Insights & reflections

This chapter set out to investigate the use of CVRs in biopharma M&A. Of all publicly announced deals in the United States in the period 2013-2023, only about 2-3% incorporate a CVR as part of their deal structure, which roughly amounts to 5-6 deals per year. Remarkably, in just the first few months of 2023, already four biopharma deals involving a CVR have been announced. The large majority of these transactions occur within the life sciences and healthcare industry because the structure of the CVR resembles the commonly used structure of a licensing deal. As a result, industry professionals are well-acquainted with milestone payments, which may lead to a greater willingness to accept the terms of an event-driven CVR. While event-driven CVR appear to have a use case in US biopharma deals, their utilization in Europe has been relatively limited. According to industry professionals, this is not due to legal barriers, but rather due to the absence of a legal precedent and more conservative approach to dealmaking.

Combined with the insights from Chapter 4, we have gathered ample information to give an elaborate answer to our main research questions: 1) What are the reasons behind the apparent upward trend in the use of CVRs? 2) Why are CVRs more often incorporated in deal structures in the US than in Europe? 3) What are the specific situations in which CVRs prove to be particularly valuable? 4) What does this emerging trend imply for financial advisers at Van Lanschot Kempen? However, prior to doing that, we will strengthen our knowledge of the various factors that shape the decision to include a CVR in the deal structure. To achieve this, a real-world case study was conducted, focusing on the acquisition of Sigilon Therapeutics by Eli Lilly & Company, announced on June 29, 2023.

6. Case study: How Lilly's CVR sweetened the Sigilon Acquisition

On June 29, 2023, Eli Lilly and Company (NYSE: LLY) and Sigilon Therapeutics, Inc. (Nasdaq: SGTX) jointly announced a definitive agreement stating that Lilly will acquire Sigilon Therapeutics (Eli Lilly & Company, 2023a). At the time of announcement, Sigilon had a share price of a mere $3.93 and market cap of less than $10m, which is below the minimum listing requirements for the Nasdaq exchange (see Exhibit 1) (Refinitiv Eikon, n.d.). The terms of the agreement stated that Lilly will acquire all outstanding shares of Sigilon for $14.92 per share in cash (a total upfront payment of approximately $34.6m). In addition, the shareholders of Sigilon Therapeutics will receive one non-tradeable CVR per share, which entitles the shareholders to an additional $111.64 per share in cash, bringing the total potential consideration to $126.56 per share in cash (a total deal value of ~$309.6m) (Eli Lilly & Company, 2023a). Remarkably, a staggering 88% of the total deal value is dependent on future events outside selling shareholders' control. Following this press release, two questions emerge: 1) What events led to such a significant drop in Sigilon Therapeutics' share price? and 2) What motivated Sigilon's shareholders to agree with these deal terms? This case study will investigate the events and decisions leading up to this acquisition.

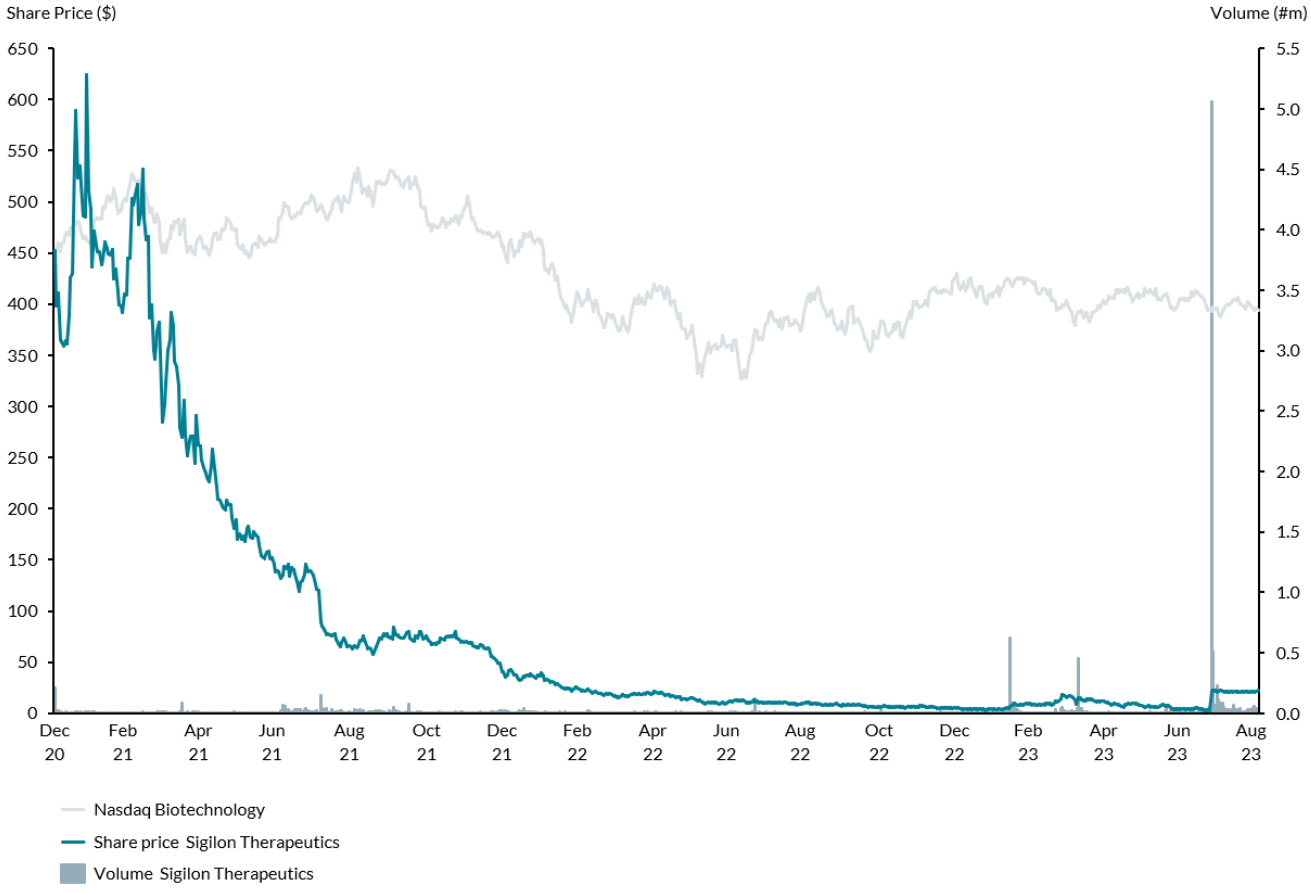

Exhibit 1 | Share price performance of Sigilon Therapeutics (NSDQ: SGTX) since its initial public offering on December 4, 2020 (Refinitiv Eikon, n.d.). *The Nasdaq Biotechnology (NBI) is rebased to Sigilon Therapeutics' share price as per December 4, 2020 ($452.14); The share price of Sigilon Therapeutics is adjusted for stock splits.*

6.1 Sigilon Therapeutics: revolutionizing protein delivery (2015 – 2017)

To obtain a comprehensive understanding of how this acquisition came about and why Sigilon chose to sell itself to Lilly, we will need to delve into the history of Sigilon Therapeutics. This study begins with unravelling the reasons behind its founding and identifying the key individuals involved. Subsequently, we will explore how Sigilon's technology works and how it differentiates from competitors.

The origins of Sigilon

In 2015, Sigilon Therapeutics was incorporated by Douglas Cole, M.D., managing partner at the US-based venture capital firm Flagship Pioneering, in conjunction with academic co-founders Robert Langer and Daniel Anderson of the Massachusetts Institute of Technology (MIT) (Sigilon Therapeutics, 2021a). Flagship Pioneering is a leading venture capital firm investing in and contributing to the development of life sciences companies (Flagship Pioneering, 2017). Since its inception, Flagship Pioneering has founded over a hundred companies, including COVID-19 vaccine producer Moderna (Nasdaq: MRNA) (Flagship Pioneering, 2017). The two academic founders have a strong track record of launching biotechnology companies as well. In addition to being co-founder of Sigilon Therapeutics, Robert Langer was co-founder of more than 25 other biotechnology companies, including Moderna (Corbyn, 2022; Sigilon Therapeutics, 2017a). Daniel Anderson was also founder of multiple biotechnology companies, including Crispr Therapeutics and Living Proof (Sigilon Therapeutics, 2017a). Together, this team of accomplished investors, founders, and scientists, made for a promising start of Sigilon Therapeutics.

During a decade worth of research, Robert Langer and Daniel Anderson conjointly developed the foundations for an encapsulated cell therapy platform called Shielded Living Therapeutics (SLTx) (Flagship Pioneering, 2017). Encapsulated cell therapy is a technology that involves placing engineered cells inside anti-fibrotic spheres, enabling them to produce therapeutic proteins of choice while being protected from immune system responses. Once fully developed, the SLTx cell therapy technology would be able to produce therapeutic proteins over sustained periods of time without triggering fibrosis, and therefore, without requiring immune suppression (Flagship Pioneering, 2017).

The first two years after the incorporation were dedicated to obtaining the intellectual property (IP) rights from MIT and further developing the technology (Flagship Pioneering, 2017). In February 2016, Sigilon obtained exclusive, worldwide, royalty-bearing rights to multiple patents through a license agreement with MIT (Sigilon Therapeutics, 2019a). In the following years, multiple amendments to the MIT License were made to lay the groundwork for a sustainable competitive advantage. Ultimately, the company managed to create a comprehensive patent portfolio of 16 patent families, covering all elements of the SLTx platform as well as therapeutic uses in important disease areas (Sigilon Therapeutics, 2019a). Most of the key patents would expire in the 2033-2038 time frame, which would give Sigilon Therapeutics approximately 20 years to develop its therapeutic candidates. After two years of preparations, on June 21, 2017, Sigilon Therapeutics was officially launched to the public, capitalized with $23.5m from Flagship Pioneering (Flagship Pioneering, 2017).

Shielded Living Therapeutics

The idea to encapsulate living cells that produce therapeutic proteins, has been around for quite some time (Sigilon Therapeutics, 2021a). Across the field of encapsulated cell therapies, one of the major challenges had been developing a matrix that prevents an immune response. Previous efforts often resulted in short-lived encapsulated cell implants due to fibrosis and inadequate

oxygen supply. Sigilon, however, claimed that their spheres, coated with a molecule called Afibromer™, would not trigger an immune response from the body (Sigilon Therapeutics, 2021a). Remarkably, the researchers in the labs of Robert Langer and Daniel Anderson had discovered a family of novel, anti-fibrotic small molecules that could be conjugated to the outer layer of an alginate (seaweed) sphere, ultimately forming the proprietary Afibromer™-coated matrix (Sigilon Therapeutics, 2021a). Furthermore, the researchers developed an inner layer consisting of a proprietary conjugation of alginates and peptides. They also determined that the optimal size for these spheres seemed to be 1.5mm, providing room for approximately 30,000-40,000 cells. Pre-clinical studies demonstrated that these carefully constructed spheres allowed an influx of essential nutrients to keep the cells alive and an efflux of the desired therapeutic proteins, while avoiding pericapsular fibrotic overgrowth on the outer surface (see Exhibit 2) (Sigilon Therapeutics, 2021a).

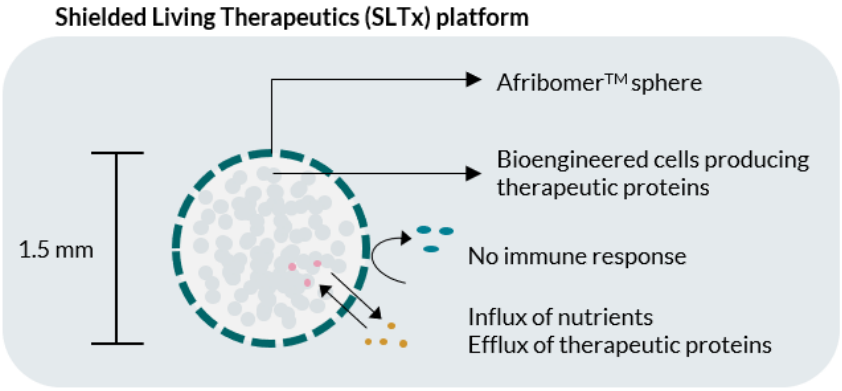

Exhibit 2 | Mechanism of action of the Shielded Living Therapeutics (SLTx) platform. The SLTx cell therapy platform consists of two main components, namely therapeutically engineered cells and the Afibromer™ coated spheres. The spheres are designed in a way that they allow influx and efflux of nutrients and therapeutic proteins, respectively. At the same time, the small molecule Afibromer™ allegedly prevents fibrosis from happening (Sigilon Therapeutics, 2021a).

The engineered cells within the SLTx platform can be designed to express a multitude of therapeutic molecules. For the majority of the product candidates, Sigilon used a human retinal pigment epithelial cell line to produce the therapeutic proteins (Sigilon Therapeutics, 2021a). This cell line was well-suited for genetic modification, exhibited macrophage-like properties for clearing cellular debris, and had demonstrated long-term survival within the SLTx spheres. On top of that, this parental cell line was especially attractive because it had been used in several Phase I and II trials before, none of which reported significant safety concerns. In addition, Sigilon was designing induced pluripotent stem cells (iPSCs), a type of stem cells derived from adult cells, to mimic the function of pancreatic islet cells. Once these engineered iPSCs were able to secrete insulin in a glucose-dependent manner, they could be used for the potential treatment of type 1 diabetes (Sigilon Therapeutics, 2021a).

Encapsulated cell therapy holds potential for the numerous diseases that characterized by the loss or malfunction of specific cells or proteins (Sigilon Therapeutics, 2021a). As demonstrated by the pre-clinical pipeline of 2017, Sigilon decided to focus its first SLTx product candidates on treatment of lysosomal storage diseases (SIG-005 and SIG-007) and rare blood disorders (SIG-001 and SIG-003) (see Exhibit 3) (Sigilon Therapeutics, 2017b). Moreover, Sigilon hypothesized that the SLTx technology could be used for more sophisticated applications, like producing insulin in response to rising glucose levels, for treatment of type 1 diabetes patients (SIG-002).

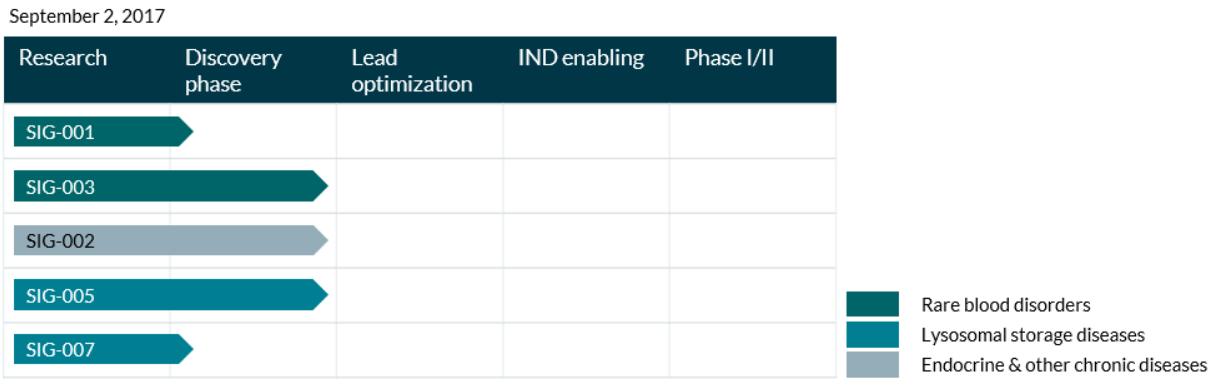

Exhibit 3 | Sigilon Therapeutics' pipeline as of September 2, 2017. At the time, specific therapeutic targets and/or disease areas were not disclosed (Sigilon Therapeutics, 2017b).

Competitive advantage of the SLTx platform

The most important feature of the SLTx platform is the fact that it could be a functional cure for chronic diseases without requiring immune suppression and without altering the host genome (see Exhibit 4) (Sigilon Therapeutics, 2021a). Conventional attempts to replace or restore malfunctioning cells or proteins, have included procedures like blood transfusions, bone marrow transplants, and replacement therapies, depending on the therapeutic indication. These therapeutic interventions have improved patient well-being, but have not been able to cure the disease or prevent the disease from progressing. Recently, researchers have focused their efforts on developing cell and gene therapies for the treatment of chronic diseases. Despite significant advancements in the field, both cell and gene therapies are associated with their own set of challenges, related to manufacturing, clinical efficacy, and safety (Sigilon Therapeutics, 2021a).

sigilon therapeutics

Feature	SLTx products	Injectable proteins	Gene therapy/editing
Alter host genome	✗	✗	✓
Durable	✓	✗	✓
Controllable exposure	✓	✓	✗
Ability to redose & retrieve	✓	✓	✗
No immune suppression	✓	✓	~
Affordable off-the-shelf	✓	✓	✗

Exhibit 4 | Comparison of the SLTx platform compared to other therapeutic approaches (adapted from Sigilon Therapeutics, 2021a).

According to Sigilon Therapeutics, the SLTx platform provides a practical solution to these issues. Sigilon's encapsulated cell therapy is administered into the peritoneal cavity under general anesthesia within 30 minutes, which is considered a minimally invasive intervention. Due to the slow turnover rate and self-renewing ability of the cells, the product candidates could provide a long-term effect of up to 3-5 years (Sigilon Therapeutics, 2021a). Moreover, preclinical studies

showed that the SLTx product candidates were redosable, retrievable, and showed consistent, dose-dependent expression of the therapeutic molecules. These features should improve the safety profile and allow for a tailored approach to fit the patients' needs.

From a business perspective, another highly attractive feature of Sigilon's encapsulated cell therapy is the modularity of the SLTx platform (Sigilon Therapeutics, 2021a). SLTx product candidates from different development programs are highly similar, apart from the customized expression cassette, which is the part responsible for producing the desired therapeutic protein. Moreover, substantial efforts have been put into developing a cost-effective manufacturing platform that would allow for truly 'off-the-shelf' products. Sigilon's products are 'off-the-shelf' because it is an allogeneic cell therapy, i.e. it relies on a single source of cells to treat all patients. As a result, this modular platform approach allowed Sigilon to build a diverse pipeline of product candidates for patients in rather distinct therapeutic areas, ranging from rare blood disorders to endocrine diseases. The company anticipated that this could result in significant synergies in manufacturing, while providing an opportunity to leverage prior (pre-)clinical studies. Ultimately, the cost of goods sold (COGS) are anticipated to be comparable to monoclonal antibodies and considerably lower than competing cell and gene therapies (Sigilon Therapeutics, 2021a).

Insights & reflections

Starting from its incorporation in 2015, Sigilon Therapeutics' first two years were marked by growth in several different areas. The first major step was assembling its founding team and laying the foundations for its board of directors. In addition, Sigilon could not have been founded without obtaining the IP licenses from MIT. These licenses provide the company with the legal rights to the SLTx platform and allow the company to maintain a competitive advantage over time. Lastly, during these initial two years, Sigilon initiated the development of the first five SLTx product candidates in three different therapeutic areas.

6.2 Tailwinds for take-off (2018 – 2020)

After the official launch of Sigilon Therapeutics in 2017, the subsequent three years were marked by strategic positioning and growth. The company expanded its leadership team, broadened its drug development pipeline into multiple therapeutic areas, and advanced its first product candidate into clinic trials. Moreover, Sigilon managed to secure a strategic partnership with a large biopharma company, which provided financing to support pipeline development. These events seemingly put Sigilon Therapeutics in a strong position for the future.

Expanding the leadership team

From the start in 2017, the company launched with an experienced leadership team (Flagship Pioneering, 2017). Prior to his role as Chief Executive Officer (CEO) of Sigilon Therapeutics, Dr. Paul Wotton took on the role as president and CEO of multiple life sciences companies, including Ocata Therapeutics, Antares Pharma, and Topigen Pharmaceuticals (Flagship Pioneering, 2017). Alongside him, a team of highly experienced professionals was assembled, including Chief Technology Officer David Peritt, Chief Strategy Officer and Head of Operations Devyn Smith, and Chief Business Officer James Watson (Flagship Pioneering, 2017). In 2018, Sigilon made significant additions to its senior team with the aim of successfully bringing their promising therapy to the market.

In January 2018, David Moller was appointed as Chief Scientific Officer (CSO) to lead the scientific development of Sigilon's technology platform (Sigilon Therapeutics, 2018a). David Moller's extensive experience in the field and his strong network made him an excellent fit for the company. Previously, Dr. Moller was Vice President at Eli Lilly and responsible for drug discovery and early drug development in diverse therapeutic areas. Dr. Moller and his team made several important additions to the pipeline, including Lilly's blockbuster diabetes drug Trulicity™ (Sigilon Therapeutics, 2018a).

> *"During my career I've been fortunate to investigate and develop several novel therapies. I'm particularly excited about the opportunity to now join a company that is poised to revolutionize the way that proteins are delivered —continually manufactured in the body by programmable cell implants — to treat numerous serious diseases."*
>
> *– David Moller, CSO of Sigilon Therapeutics (January 4, 2018)*

In August 2018, just a year after the company's launch, CEO Paul Wotton stepped down due to a family health issue and was succeeded by Rogerio Vivaldi, who not only had experience as a former treating physician but also as Chief Global Therapeutics Officer at Bioverativ and Chief Commercial Officer at Spark Therapeutics (Sigilon Therapeutics, 2018b). Later that year, the senior management team expanded with the addition of four key members: Deya Corzo as Chief Medical Officer, Olivia Kelly as Vice President of Islet Cell Therapy Research, Vanya Sagar as Vice President of HR, and Martha Roko as Head of Manufacturing (Sigilon Therapeutics, 2018c). Together with the existing management team, these individuals played pivotal roles in driving Sigilon Therapeutics' growth.

A partnership of a lifetime

A mere three months after David Moller – former Vice President at Eli Lilly – was appointed CSO, Sigilon Therapeutics announced a global collaboration with Eli Lilly and Company (NYSE: LLY) to develop SLTx encapsulated cell therapies for the potential treatment of type 1 diabetes (Sigilon Therapeutics, 2018d). Eli Lilly is a US-based pharmaceutical company founded in 1876, with a

market capitalization of $500.4bn (as of August 9, 2023). Lilly is a leading player in the field of diabetes, oncology, immunology, and neuroscience (Eli Lilly & Company, 2023b). In 2022, over 50% of total revenues came from the sale of diabetes drugs. More specifically, 26.1% of total revenue was generated by the sale of its diabetes blockbuster drug Trulicity™, which returned $5,688.8bn sales in the United States and $1,750.9bn sales outside the United States (Eli Lilly & Company, 2023b).

Despite its position as market leader, Lilly faces relentless competition in the sizeable and profitable diabetes market. To illustrate, in 2017, the large biopharma company Novo Nordisk attempted to capture a part of Lilly's market share by conducting head-to-head trials comparing their novel compound to Eli Lilly's Trulicity™ (Staton, 2017). Moreover, key patents associated with Trulicity™ are expected to expire between 2027 and 2029, after which generic competition is anticipated to enter the market (Higgins-Dunn, 2021). To stay ahead of competitors and to offset the losses that will occur following the patent expirations, Lilly continuously needs to leverage its dynamic capabilities. This means actively developing new assets through internal innovation, and identifying and acquiring emerging technologies via external innovation (see Chapter 4.2) (Ernst & Young, 2020). Two options for Eli Lilly to pursue an external innovation are to acquire emerging biopharma companies or to form strategic partnerships, like the Lilly-Sigilon partnership.

> *"At Lilly, we endeavor to change the frontiers of what's possible in medicine, both through our own scientific labs and in collaboration with other leading researchers. We are excited to be collaborating with, and investing in, Sigilon as they seek to develop encapsulated cell therapies, a potentially disruptive technology that could result in meaningful clinical advancements for chronic diseases such as type 1 diabetes."*
>
> *– Daniel Skovronsky, Senior Vice President for Clinical and Product Development at Eli Lilly (April 4, 2018)*

In the Lilly-Sigilon partnership, Sigilon was responsible for creating pre-clinical product candidates consisting of iPSCs that function as the insulin-producing pancreatic islets of Langerhans, encapsulated in Afibromer™-coated spheres for the treatment of type 1 diabetes (Sigilon Therapeutics, 2018d). One of these SLTx candidates was SIG-002 program. In terms of responsibilities, Sigilon was going to be in charge of all the development activities and costs for the pre-clinical phase until they submit an investigational new drug (IND) application. Once the IND would be submitted, Lilly would take over and carry out all the clinical development and commercialization efforts (Sigilon Therapeutics, 2018d). Lilly is an excellent partner for the clinical development of the SIG-002 program, as they are an important player in the field of diabetes, with expertise in developing and commercializing therapeutic interventions for this indication. In contrast, Sigilon lacks the know-how required for clinical development, and acquiring such expertise would involve significant investments. Moreover, this partnership sends a positive signal to the market, underscoring that Lilly recognizes the strong potential of the SIG-002 program and of Sigilon's technology.

The terms of the partnership agreement state that Lilly will obtain the full rights to Sigilon's encapsulation technology specifically for insulin-producing beta cells. In return, Sigilon will receive an upfront payment of $63 million, up to $165m in regulatory milestones, up to $250m in sales-based milestones, and mid-single to low-double digit royalties on future sales (see Exhibit 5) (United States Securities and Exchange Commission, 2020; Sigilon Therapeutics, 2018d). In addition, Lilly will make a $13.1m equity investment in exchange for 3,500,000 shares of Series A-

3 convertible preferred stock. This partnership clearly demonstrates Sigilon's intended business model, namely that of asset creation and out-licensing (see Chapter 5.1).

Timing	Proceeds
Upfront payments	$63 million $13.1 million equity investment
Future payments	$165 million regulatory milestones $250 million sales-based milestones Mid-single to low-double digit royalties

Exhibit 5 | Overview of Sigilon's proceeds from the Lilly-Sigilon partnership (United States Securities and Exchange Commission, 2020).

The asset creation and out-licensing business model involves developing innovative assets using Sigilon's technology and then licensing them to large biopharma companies for further development and commercialization. This business model allows Sigilon to generate upfront cash payments from partners, which in turn enable the company to sustain their ongoing research and product development efforts. Moreover, this business model aligns seamlessly with Sigilon's highly modular platform. The modular approach enables Sigilon to quickly develop assets that either fit their own strategic ambitions or that suit the specific demands of potential partners, e.g. diabetes assets for Lilly. After closing their first partnership with Eli Lilly, Sigilon was well-funded and ready to advance and expand the pipeline.

Sigilon's platform modularity enabled rapid pipeline expansion

From its launch in 2017 till the end of 2020, Sigilon Therapeutics managed to expand its pipeline significantly. In 2017, with the $23.5m in capital from Flagship Pioneering, Sigilon Therapeutics initiated the preclinical development of five programs, namely SIG-001 (Hemophilia A), SIG-002 (type 1 diabetes), SIG-003 (Hemophilia B), SIG-005 (MPS-1), and SIG-007 (Fabry disease) (see Exhibit 8) (Sigilon Therapeutics, 2017b). By the end of 2020, with the capital infusion of $76.1m from Eli Lilly, Sigilon successfully broadened its pipeline with four additional assets: SIG-009 (FVII Deficiency), SIG-018 (MPS-2), SIG-015 (Immune-mediated diseases), and SIG-020 (MPS-6) (see Exhibit 6) (Sigilon Therapeutics, 2021a).

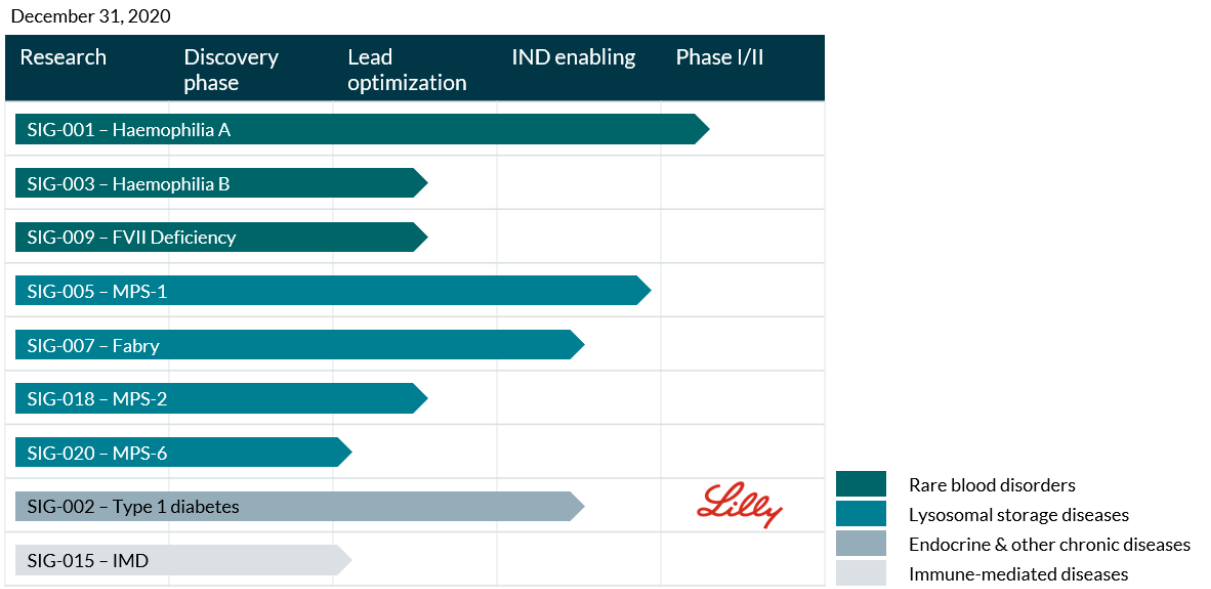

Exhibit 6 | Overview of Sigilon Therapeutics' pipeline as of December 31, 2020 (adapted from Sigilon Therapeutics, 2021a). Compared to the pipeline of September 2, 2017 (Exhibit 3), four programs were added, namely SIG-009, SIG-018, SIG-020, and SIG-015. SIG-001 advanced from discovery phase to Phase I/II clinical trial. Programs SIG-005, SIG-007, and SIG-002 progressed from discovery phase to IND-enabling phase. *MPS-1: Mucopolysaccharidosis I (Hurler Syndrome); MPS-2: Mucopolysaccharidosis II (Hunter syndrome); MPS-6: Mucopolysaccharidosis VI (Maroteaux-Lamay syndrome); IMD: Immune-mediated diseases.*

Lead asset SIG-001

Sigilon decided to advance SIG-001 for treatment of Hemophilia A as its lead asset, because it represents a sizeable market where encapsulated cell therapy could provide clinical benefit. Hemophilia A and B are rare, inherited blood disorders caused by a partial or total deficiency of coagulation factor VIII or IX, respectively (Marchesini, Morfini, & Valentino, 2021). Based on their factor levels, Hemophilia patients can be categorized into having severe (factor activity < 1%), moderate (factor activity 1-5%), and mild (factor activity 5-49%) disease (National Bleeding Disorders Foundation, n.d.). The clinical presentation differs significantly between patients. People with severe Hemophilia A often experience spontaneous bleeding into joints or muscles, whereas people with moderate or mild disease suffer primarily from trauma-induced bleeding (National Bleeding Disorders Foundation, n.d.). Hemophilia A affects approximately 30,000 males both in the United States and in the European Union (European Medicines Agency, 2022; National Bleeding Disorders Foundation, n.d.). Traditionally, the treatment for Hemophilia A has been lifelong factor replacement therapy, which had to be administered one or more times per week or per month (European Medicines Agency, 2022).

In 2017 and 2018, a novel bispecific monoclonal antibody called Hemlibra received approval for the majority of Hemophilia A patients in the United States and the European Union (Helfand, 2018). Hemlibra achieved significant annual sales, reaching approximately $1.6 billion in 2019 and about $2.5 billion in 2020, demonstrating the market size (Roche, 2021). While Hemlibra represented a substantial improvement for Hemophilia A patients in terms of clinical efficacy, it is important to note that it does not provide a complete cure and still requires subcutaneous administration every one, two, or four weeks (Helfand, 2018). These insights highlight that Hemophilia A represents a sizeable market with an ongoing clinical need for more effective treatments.

In 2020, multiple biopharma companies were trying to establish a presence in the Hemophilia A market by developing innovative treatments for patients. For example, several viral gene therapies were undergoing Phase III clinical trials, including Roctavian from BioMarin (NCT04323098), SB-525 from Pfizer/Sangamo (NCT03587116), and SPK-8011 from Roche/Spark (NCT03432520) (Sigilon Therapeutics, 2021a). It is worth noting that even if these therapies did manage to obtain FDA approval, several issues related to gene therapies would remain, including unknown durability, limited possibility of redosing, existing immunity against adeno-associated viral (AAV) vectors, and high COGS (Sigilon Therapeutics, 2021a). Sigilon's encapsulated cell therapy could present as an alternative option, surmounting these challenges.

Sigilon's SIG-001 is an encapsulated cell therapy designed to produce adequate levels of factor VIII for at least a couple of years (Sigilon Therapeutics, 2019b). In August 2019, Sigilon Therapeutics earned Orphan Drug Designation for SIG-001. One year later, in August 2020, the FDA accepted the IND submission, and by May 2020, the UK granted clinical trial authorization (Sigilon Therapeutics, 2021a). Subsequently, in the fourth quarter of 2020, the first two Hemophilia A patients were dosed with SIG-001 in a Phase I/II clinical trial. The Phase I/II clinical trial (NCT04541628) was a multi-center, open-label, dose escalation study to evaluate the safety, tolerability, and preliminary efficacy of SIG-001 in adults with severe or moderate Hemophilia A. The initial results of the first two patients showed that SIG-001 therapy led to low-to-mid-single digit factor levels, falling below the minimal threshold of 20% required to prevent joint bleedings (Marchesini et al., 2021; Sigilon Therapeutics, 2021a). Nevertheless, these data provided an initial proof-of-concept and no serious adverse events were reported (Sigilon Therapeutics, 2021a). In response, Sigilon began making improvements to the manufacturing process in Q1 2021 to enhance cell potency and function. The company anticipated having up to nine months of follow-up data for 3-4 patients by Q3 2021, and the enrolment phase of the Phase I/II study was on track to be completed before the end of 2021 (Sigilon Therapeutics, 2021a).

SIG-005

Apart from advancing their lead asset, SIG-001 for Hemophilia A, and the partnered asset, SIG-002 for type 1 diabetes, the company simultaneously worked on developing seven additional assets, highlighting the modularity of the SLTx platform. Notably, by the end of 2020, one of these assets, SIG-005, had progressed to the stage where it was almost ready for IND submission.

SIG-005 was designed to treat patients with mucopolysaccharidosis type I (MPS-1), also known as Hurler Syndrome, which is a genetic disease resulting from a deficiency in the lysosomal enzyme α-L-iduronidase (IDUA). The standard treatment options for individuals with this progressive lysosomal storage disorder include hematopoietic stem cell transplants and enzyme replacement therapy (Sigilon Therapeutics, 2021a). In December 2020, Sigilon announced that SIG-005 had received Orphan Drug Designation from the FDA for treatment of MPS-1 (Sigilon Therapeutics, 2020a). The first patients were anticipated to receive doses in a Phase I/II trial in the second half of 2021 (NCT05665036). Furthermore, the company submitted clinical trial applications in the UK and Brazil in June and July 2021, respectively (Sigilon Therapeutics, 2021b).

Insights & reflections

At this point in the case study, we have obtained a clear picture of Sigilon Therapeutics' business case (see Exhibit 7). On the upside, Sigilon Therapeutics can leverage a number of strengths and opportunities. First, the company offers a highly modular platform that, once de-risked, can be rapidly expanded into different chronic disease areas. This means that, after obtaining approval, the company could tap into a sizeable market and generate substantial sales. Moreover, the number of people living with chronic disease is expected to increase due to changes in

demographics, suggesting that Sigilon is targeting a growing market (Atella et al., 2019; Mobasseri et al., 2020). Second, the modularity of the platform is enhanced by the 'off-the-shelf' manufacturing process, which not only improves efficiency but also reduces costs. Sigilon's encapsulated cell therapy is anticipated to have lower COGS than existing cell and gene therapies, providing it with a competitive advantage and potentially shielding it from the impacts of regulatory changes like the IRA (see Chapter 4.3). Third, the company benefits from a strong network of stakeholders. Sigilon is backed by a renowned venture capital firm and has secured a strategic partnership with Lilly, emphasizing the company's potential and the strength of its technology. In addition, once the technology is de-risked, Lilly might be open to expanding the partnership into different disease areas. Lastly, Sigilon Therapeutics is led by an experienced leadership team and supported by a trustworthy board of directors and scientific advisory board.

On the downside, Sigilon Therapeutics has a number of weaknesses and threats to overcome. First, the company relies heavily on the success of one technology that has not yet been fully de-risked. Although the company decreases risk by diversifying into multiple disease areas, it does not diversify its risk across different technologies. Historically, encapsulated cell therapies have proven challenging to develop, with previous attempts showing limited success. Currently, the technology has shown limited efficacy, with factor-levels below the required threshold of 20%, indicating a need for improvement. In addition, the therapeutic intervention itself is rather invasive, requiring intraperitoneal administration, which might not be appealing to all patients. Second, the biopharma industry is highly competitive, particularly areas like Hemophilia A and type 1 diabetes. Third, changes in market conditions or regulations may negatively affect Sigilon's ability to raise capital or to bring its products to the market, respectively.

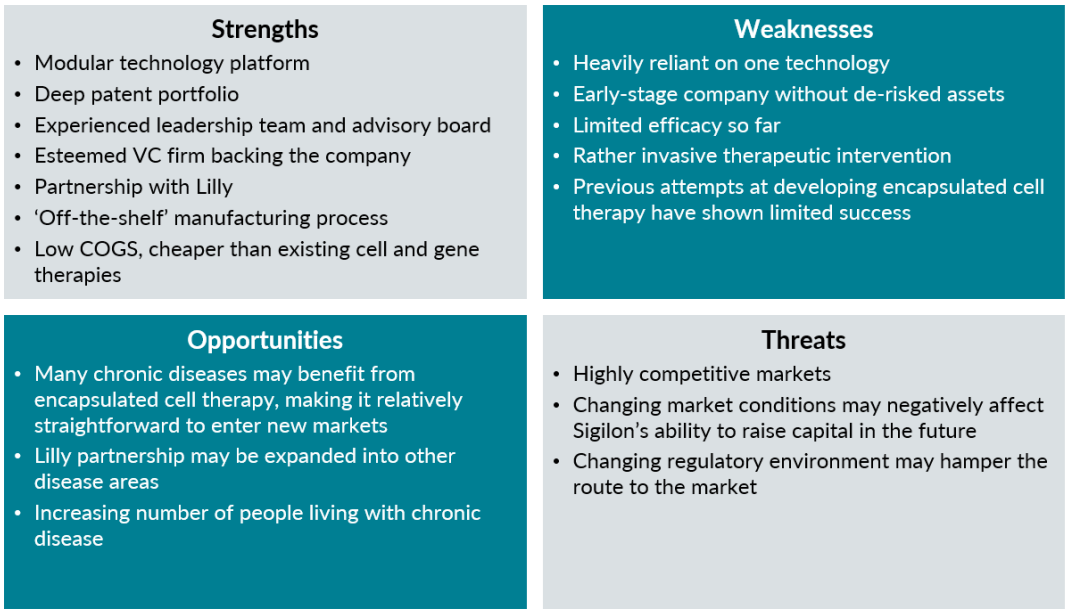

Exhibit 7 | Analysis of Sigilon Therapeutics' strengths, weaknesses, opportunities, and threats as of 2020.

In summary, from 2017 to 2020, Sigilon Therapeutics achieved significant milestones. The company managed to expand its pipeline from five to nine assets and established a long-lasting partnership with Lilly. Looking ahead, once the SLTx product candidates start showing positive data, it could de-risk the technology and enhance the overall value of both the platform itself and the pipeline as a whole. This period of progress ultimately resulted in a positive momentum surrounding Sigilon Therapeutics, facilitating and reinforcing the process of raising capital in 2020.

5.3 The glory days (2020 – 2021)

In the years leading up to 2021, Sigilon Therapeutics propelled it pipeline forward, successfully developing and advancing several assets. Despite not generating any revenue, the company had to invest significant resources into R&D. Recognizing the need for additional financing, the company set out to raise capital in 2020. Fortunately, the positive momentum surrounding the company and the favorable market conditions enabled easy access to capital.

Private fundraising

Emerging biopharma companies like Sigilon often rely heavily on equity financing to fund their R&D investments (see Chapter 4.2). Thanks to the Series A financing round and the contributions from the Lilly-Sigilon partnership, the company managed to expand and advance the pipeline. However, as SIG-001 approached the final stages of the pre-clinical studies, the company had to raise additional capital to fund the first-in-human Phase I/II study (Sigilon Therapeutics, 2020b). Fortunately, Sigilon's business case (see Exhibit 7), including its founding team, market opportunity, and competitive advantage, was attractive enough for investors to make it worth the bet.

On March 17, 2020, the company announced the completion of a Series B financing round, ultimately raising a considerable $80.3m to advance SIG-001 into the clinic and to progress the rest of the pipeline (Sigilon Therapeutics, 2020b). Investors participating in this Series B financing round were Canada Pension Plan Investment Board (CPP Investments), Longevity Vision Fund, BlackRock, and existing investors, including Flagship Pioneering and Lilly (Sigilon Therapeutics, 2020b). In addition to the 3,500,000 shares of Series A-3 convertible preferred stock purchased for $13.1m in 2018 ($3.75 per share), Lilly bought 2,000,000 of Series B convertible preferred stock for approximately $12.0m ($6.00 per share) (United States Securities and Exchange Commission, 2020; Sigilon Therapeutics, 2021a). Later, in October 2020, Sigilon completed a Series B-1 financing round of 3,550,000 of convertible preferred stock at $7.00 per share, bringing the total Series B-1 proceeds to $24.9m. The completion of this round brough Sigilon's total funding to more than $225m (United States Securities and Exchange Commission, 2020).

> *"The near-term transition to clinical development and the platform's breadth and progress reflect the power and productivity of Sigilon's approach. Successful conclusion of this Series B financing puts the company in a strong position to build further value."*
>
> *– Douglas Cole, Managing Partner at Flagship Pioneering and Chairman of the Board at Sigilon (March 17, 2020)*

Initial public offering

Undoubtedly fueled by the positive market sentiment, Sigilon Therapeutics decided to pursue an IPO. On December 3, 2020, Sigilon announced the pricing of the IPO and as of December 4, 2020, Sigilon's common stock started trading under the symbol "SGTX" on the Nasdaq Global Select Market exchange (Sigilon Therapeutics, 2020c). Ultimately, on December 8, 2020, the company announced the closing of their upsized IPO. The Joint Bookrunners Morgan Stanley, Jefferies, Barclays, and Canaccord Genuity had managed to sell 8,050,000 shares of common stock at a public offering price of $18.00 per share, which resulted in an aggregate gross proceeds of $144.9m, before deducting offering expenses. Several incentives may have driven Sigilon's decision to go public, including liquidity, monetization, growth capital, and equity capital market access (Rosenbaum & Pearl, 2020).

Going public provides Sigilon's existing shareholders with an opportunity to monetize on their investments. Typically, venture capital firms, such as Flagship Pioneering, adhere to the principle of "letting their winners run" to compensate for the inherent losses across their portfolio (Taylor, 2023). This strategy entails allowing the most successful investments to continue to grow, thereby offsetting the performance of other, less successful ventures. An IPO can be an ideal exit strategy in this context, offering a future liquidity event for its major shareholder Flagship Pioneering (48.3%) and other shareholders to capitalize on their investments (United States Securities and Exchange Commission, 2020).

Sigilon's major shareholders initially opted to retain large parts of their stakes in the company, underscoring their belief in the company's potential upside (see Exhibit 7). Upon closing of the IPO, all of the Series A-3 and Series B convertible preferred stock were converted into shares of common stock (United States Securities and Exchange Commission, 2020). Several investors who participated in the private funding round, including Lilly, CPP, and BlackRock, stayed aboard during the IPO. After the IPO, Sigilon's major shareholders were Flagship Ventures (33.0%), Eli Lilly (8.7%), Daniel Anderson (7.1%), and Robert Langer (7.1%). The existing shareholders of Sigilon agreed to a lock-up period after the IPO, which prevented them from monetizing on their shares for 180 days (United States Securities and Exchange Commission, 2020).

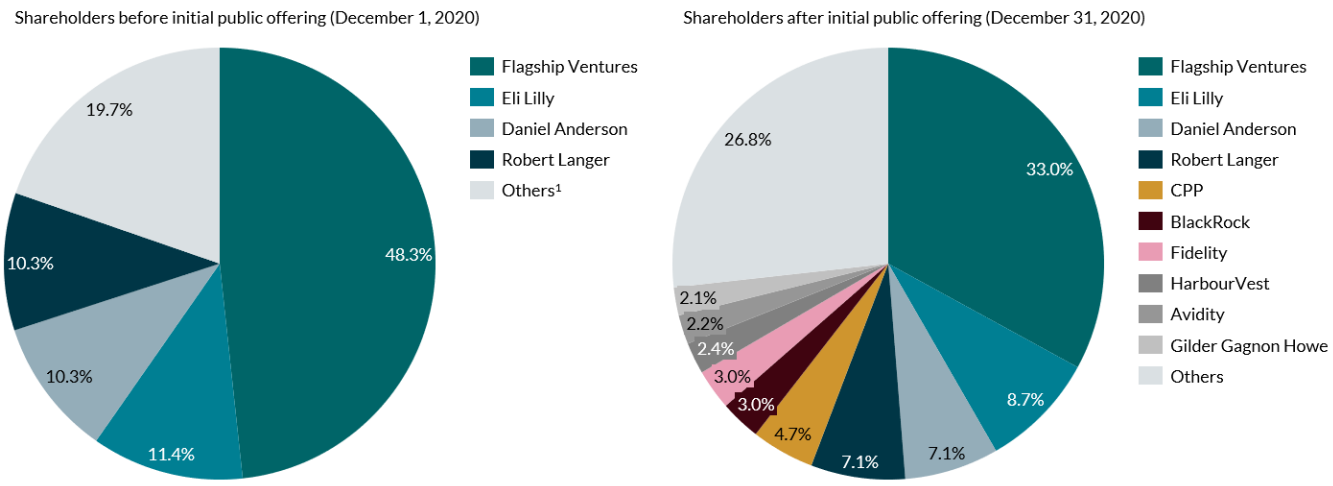

Exhibit 7 | Overview of Sigilon Therapeutics' shareholder before and after the initial public offering (United States Securities and Exchange Commission, 2020; Refinitiv Eikon, n.d.). *[1]Shareholders with less than 5% ownership, including executive officers and directors.*

Other factors driving the decision to go public may have been obtaining growth capital and accessing capital market access (Rosenbaum & Pearl, 2020). Up until the IPO, Sigilon funded their business with capital from the sale of convertible preferred stock, the Lilly-Sigilon partnership, and from borrowings under their credit facilities, generating a total funding of more than $225m (United States Securities and Exchange Commission, 2020). Nevertheless, additional funding was needed to sustain Sigilon's operational activities and to pursue its growth ambitions. Following the IPO, as of December 31, 2020, Sigilon's cash position was $202.2m. The proceeds of the IPO were allocated to progress the Phase I/II trial of SIG-001 in Hemophilia A patients, to conduct IND-enabling studies, to continue to scale the manufacturing processes, to advance the SLTx platform and other programs, and to fund working capital and general corporate costs (United States Securities and Exchange Commission, 2020).

Although an IPO offers several advantages, including liquidity and access to capital markets, it also comes with certain drawbacks. Amongst others, the stringent regulatory requirements imposed on public companies by the Securities and Exchange Commission demand meticulous reporting and transparency, resulting in an additional administrative burden and costs. Sigilon Therapeutics qualified as an 'Emerging Growth Company' and a 'Smaller Reporting Company', which allowed the company to take advantage of reduced disclosure and other requirements (United States Securities and Exchange Commission, 2020). Moreover, while an IPO can generate significant value for its shareholders, it also introduces dilution, i.e. the ownership stakes of shareholders decreases upon issuing of new shares. Lastly, the intense scrutiny from shareholders, analysts, and the market at large can prompt a short-term focus, potentially diverting attention from the company's long-term strategic objectives. Following the IPO, in January 2021, multiple equities research analysts at leading investment banks initiated coverage of Sigilon. This often coincides with increased trading volume and investor interest.

Insights & reflections

All in all, at the beginning of 2021, a sense of optimism and accomplishment surrounded Sigilon Therapeutics. Having successfully conducted an upsized Series B financing round and an upsized IPO in the same year, Sigilon became ready to complete its first-in-human trial and to advance the rest of its pipeline. Fueled by a positive momentum and supported by optimistic analysts, Sigilon was well-positioned to bring their functional cures to the clinic.

6.4 Adversity strikes (2021 – 2023)

So far, Sigilon Therapeutic has shown all the signs of a promising biopharma success story. Yet, as we delve into this chapter, we will explore the pivotal moment that changed the trajectory of Sigilon. With sufficient cash on the balance and multiple assets getting ready for clinical trials, the case takes an unexpected turn that will challenge Sigilon's path to success.

Serious adverse events

Not long after its successful IPO in December 2020, adversity struck. On July 9, 2021, Sigilon Therapeutics published a press release stating that the FDA had placed the Phase I/II trial of SIG-001 in Hemophilia A patients (n=3) on hold (Sigilon Therapeutics, 2021c). The clinical hold was a result of Sigilon reporting a serious adverse event (SAE) in a patient treated with the SLTx candidate. The last patient, who had been administered the highest dose of the treatment, developed inhibitors against Factor VIII. Antibodies targeting the exogenous Factor VIII is a well-known complication of FVIII therapy (Sigilon Therapeutics, 2021c). The development of inhibitors in Hemophilia A patients is associated with considerable morbidity, including more frequent bleedings, increased disability, and decreased quality of life (Witmer & Young, 2013). In response to this SAE, the FDA requested additional research on the potential underlying cause of the development of inhibitors, including family history and recent vaccinations (Sigilon Therapeutics, 2021c; Witmer & Young, 2013). As follows from Vivaldi's statement, it was unclear what had caused the development of inhibitors.

> *"Patient safety is our top priority, and we are encouraged that the patient is recovering. In collaboration with the regulatory agencies and our advisors, we are conducting a thorough investigation of this event* ***to confirm whether there was a causal relationship between the development of inhibitors and SIG-001****. We are committed to working with the FDA to resolve the clinical hold."*
>
> *– Rogerio Vivaldi, CEO of Sigilon Therapeutics (July 9, 2021)*

Either the company remained confident that their technology did not induce fibrosis or they hid their suspicions from the public. For quite some time after the clinical hold, the company kept on reporting about the progress of other product candidates. On August 10, 2021, the company reported that it was still awaiting clinical trial approval from the Brazilian agencies and that it planned on submitting an IND application to the FDA for their SIG-005 candidate (Sigilon Therapeutics, 2021d). Moreover, on September 9, 2021, Sigilon reported that it had received approval from the British authorities to initiate a Phase I/II trial of SIG-005 in MPS-1 patients in H2 2021 (Sigilon Therapeutics, 2021e).

On November 29, 2021, the long-awaited truth was finally revealed. Sigilon Therapeutics reported that the patient who had developed inhibitors had undergone a laparoscopic procedure to retrieve the implanted spheres (Sigilon Therapeutics, 2021f). Upon inspection of the spheres, the researchers concluded that, against expectations, the SIG-001 spheres had fibrosed and that the FVIII-producing cells were no longer alive (Sigilon Therapeutics, 2021f). These findings raised concerns about the underlying technology's effectiveness, suggesting it may not be as robust as initially believed. This discovery casted a shadow over all the other programs and impacted the timing of the initiation of the Phase I/II trial examining SIG-005 in MPS-1 patients (Sigilon Therapeutics, 2021f).

New year's resolutions

In light of these unexpected findings, Sigilon Therapeutics faced an important decision. On December 13, 2021, the company announced a strategic reprioritization that would redefine its future direction (Sigilon Therapeutics, 2021g). The company decided to reprioritize its pipeline by focusing its efforts solely on MPS-1, diabetes, and platform optimization, and by eliminating the SLTx candidates being developed for rare blood disorders (SIG-001, SIG-003, and SIG-009) and immune-mediated diseases (SIG-015) (see Exhibit 8) (Sigilon Therapeutics, 2022a). Moreover, the company did not anticipate to initiate the Phase I/II trial of SIG-005 in MPS-1 patients until further investigation was completed. Accordingly, the company chose to cut its workforce by about 38%, primarily in research, manufacturing, and administrative roles (Sigilon Therapeutics, 2021g).

This decision was anticipated to reduce Sigilon's expenses and to extend its cash runway (Sigilon Therapeutics, 2021g). As of December 31, 2021, Sigilon expected that their cash, cash equivalents and marketable securities of $123.4m, would be sufficient to fund their operational costs, capital expenditures, and debt obligations into 2024 (Sigilon Therapeutics, 2022a). Regardless, Sigilon Therapeutics would need to raise additional capital in the new year or else they would be forced to delay, reduce, or terminate their R&D programs.

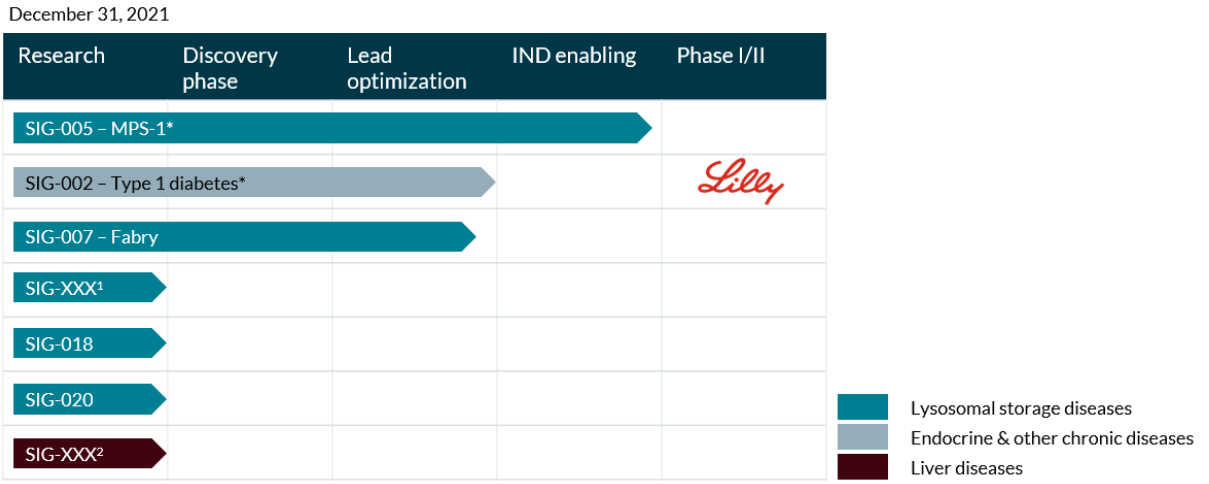

Exhibit 8 | Overview of Sigilon Therapeutics' pipeline after reprioritization in December 2021 (adapted from Sigilon Therapeutics, 2022a). Compared to the pipeline of December 31, 2020 (Exhibit 6), four programs were terminated, namely SIG-001, SIG-003, SIG-009, and SIG-015. SIG-XXX[1] and SIG-XXX[2] were added to the pipeline. **Prioritized areas of development; [1]SLTx candidate being developed for treatment of MPS-1, including treatment of central nervous system (CNS) involvement; [2]SLTx candidate being developed for treatment of liver disease.*

Back to the drawing board

In the year 2022, Sigilon's focus was directed towards conducting preclinical studies aimed at evaluating the so-called pericapsular fibrotic overgrowth (PFO) observed in the Phase I/II trial of SIG-001 in Hemophilia A patients (Sigilon Therapeutics, 2022a). During these studies, the company successfully identified ways to enhance their proprietary cross-linking chemistry and created certain prediction methods to assess the potential PFO response to SLTx products. These practical insights were then applied to optimize the SLTx platform and were integrated into the preclinical studies that were being conducted on SIG-005 (Sigilon Therapeutics, 2022b, 2022c).

*"**During the second quarter, we remained focused on completing the preclinical work that will help shape our clinical strategy moving forward.** We are presently conducting numerous preclinical studies designed to further evaluate the pericapsular fibrotic overgrowth observed in our hemophilia program. Based on the results of these novel experiments, we will determine the next best steps to leverage the full potential of our MPS-1 program and other product candidates and to continue the optimization of our platform."*

– Rogerio Vivaldi, CEO of Sigilon Therapeutics (August 4, 2022)

Throughout 2022, the company kept reporting about the initiation of a Phase I/II trial for SIG-005 as treatment of MPS-1 patients in the UK and Brazil, along with the submission of an IND application for SIG-005 in the United States. They also continued reporting about their plans to carry out IND-enabling studies for SIG-002 in 2023 (Sigilon Therapeutics, 2022b). However, nearing the close of 2022, Sigilon made a significant shift by disclosing their decision to withdraw clinical trial applications for SIG-005. Instead, they revealed their intentions to conduct IND-enabling research for an optimized MPS-1 program in H2 2023 (Sigilon Therapeutics, 2022d). As the calendar turned to the first quarter of 2023, a pivotal decision was made: Sigilon opted to discontinue its SIG-005 program entirely (see Exhibit 9). This strategic choice aimed to prioritize the advancement of it partnered asset SIG-002, the type 1 diabetes candidate, and most crucially, to conserve the company's capital reserves (Sigilon Therapeutics, 2023a).

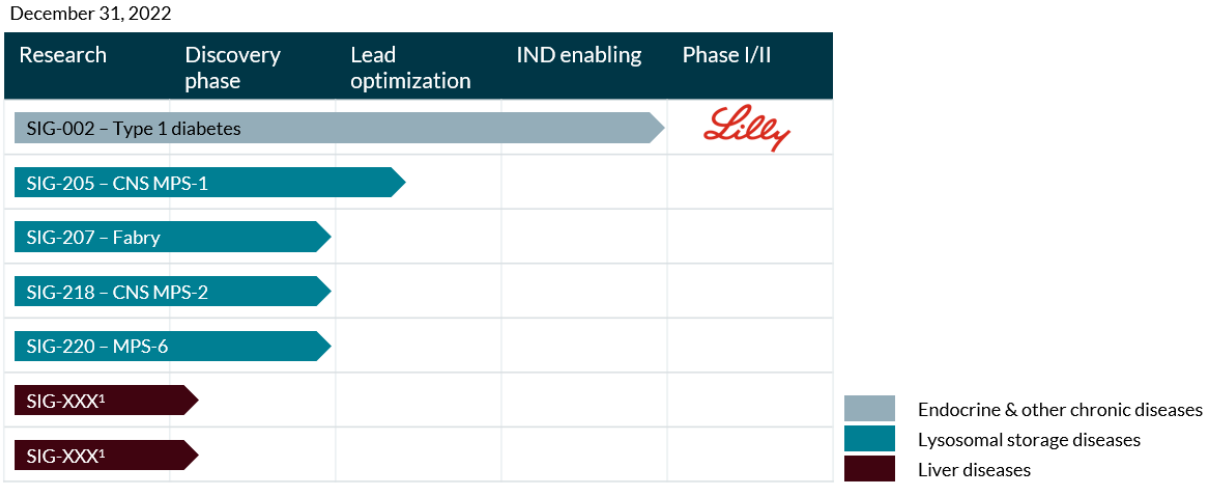

Exhibit 9 | Overview of Sigilon Therapeutics' pipeline as of December 31, 2022 (adapted from Sigilon Therapeutics, 2023a). Compared to the pipeline of December 31, 2021 (Exhibit 8), all programs were terminated, apart from the SIG-002 program for type 1 diabetes. Four new programs were initiated, namely SIG-205, SIG-207, SIG-218, and SIG-220. [1] *Undisclosed SLTx candidates being developed for treatment of liver disease.*

"I am truly excited about the direction of our SIG-002 program, including our early preclinical efficacy and durability data – which we believe is unparalleled in comparison to the published data for other programs. We believe our focused development strategy will help conserve resources and extend our cash runway into 2025, enabling us to successfully perform the activities needed to advance SIG-002 into the clinic, with an expected IND submission in 2024, and build upon the early successes of this program."

– Rogerio Vivaldi, CEO of Sigilon Therapeutics (March 14, 2023)

Facing financial headwinds

As highlighted in the 2021 annual report, the company faced the prospect of delaying, reducing, or terminating its R&D initiatives, if it failed to secure additional capital in 2022. Unfortunately, the company was unable to raise capital, probably reflecting declining investor interest in Sigilon's technology. To extend their available funds, the company had to reduce their R&D expenditures, starting from the fourth quarter of 2021 (see Exhibit 10).

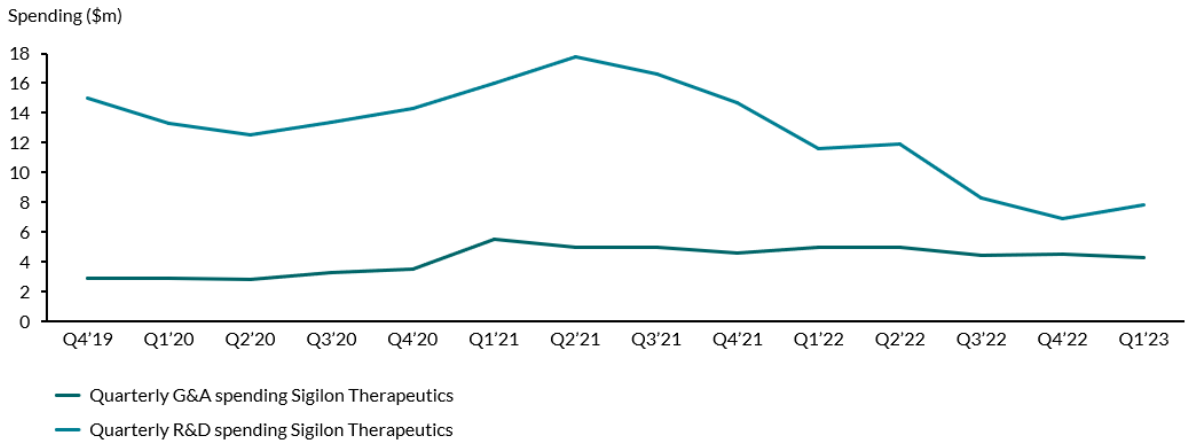

Exhibit 10 | Overview of Sigilon Therapeutics' spending as reported in the company's quarterly filings. *G&A: General and Administrative; R&D: Research and Development.*

By the close of 2021, the company had forecasted that their financial resources would carry them through to 2024 (Sigilon Therapeutics, 2022a). However, at the onset of the first quarter in 2023, Sigilon Therapeutics had a mere $56.4m in cash reserves, and a market capitalization of $30.3m (Sigilon Therapeutics, 2023b). Based on the average cash outflow of the three most recent quarters, it became apparent that Sigilon's available funds would be depleted by 2024 (see Exhibit 11). At this point in time, Sigilon found itself among the more than 200 US biopharma companies trading below cash (William Blair, 2023).

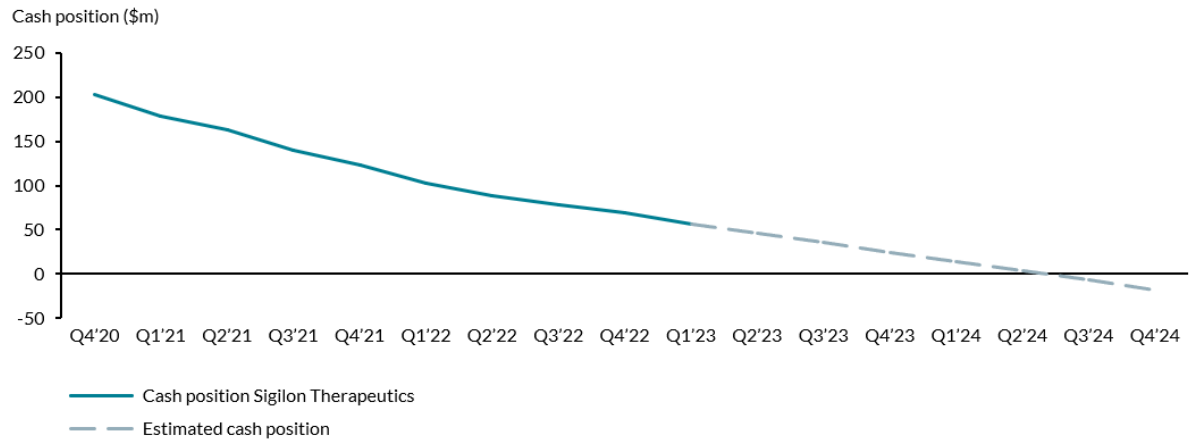

Exhibit 11 | Overview of Sigilon Therapeutics' cash position as reported in the company's quarterly filings. The estimated cash position starting from Q2'23 is calculated using the average cash outflow from Q3'22, Q4'22, and Q1'23.

The deterioration of both Sigilon's R&D programs and its financial position, did not go unnoticed by the public (see Exhibit 12). The company's stock price faced difficulties after the initial two treated patients failed to exhibit factor levels surpassing the critical threshold of around 15%. Following the clinical hold and strategic reprioritization, the share price experienced further decline. Ultimately, Sigilon's market capitalization declined to a little less than $10m and its share price fell below the minimum price requirement for continued listing on the Nasdaq Global Select Market ($1.00), which necessitated for a 1-for-13 reverse stock split on May 23, 2023 (Sigilon Therapeutics, 2023c). A reverse stock split involves consolidating a certain number of existing shares into a smaller number of new shares, artificially raising the share price. By undergoing this reverse stock split, Sigilon intended to artificially increase its share price to meet the Nasdaq's listing criteria and maintain its presence on the exchange. Sigilon Therapeutics needed to take decisive actions to escape from this precarious position.

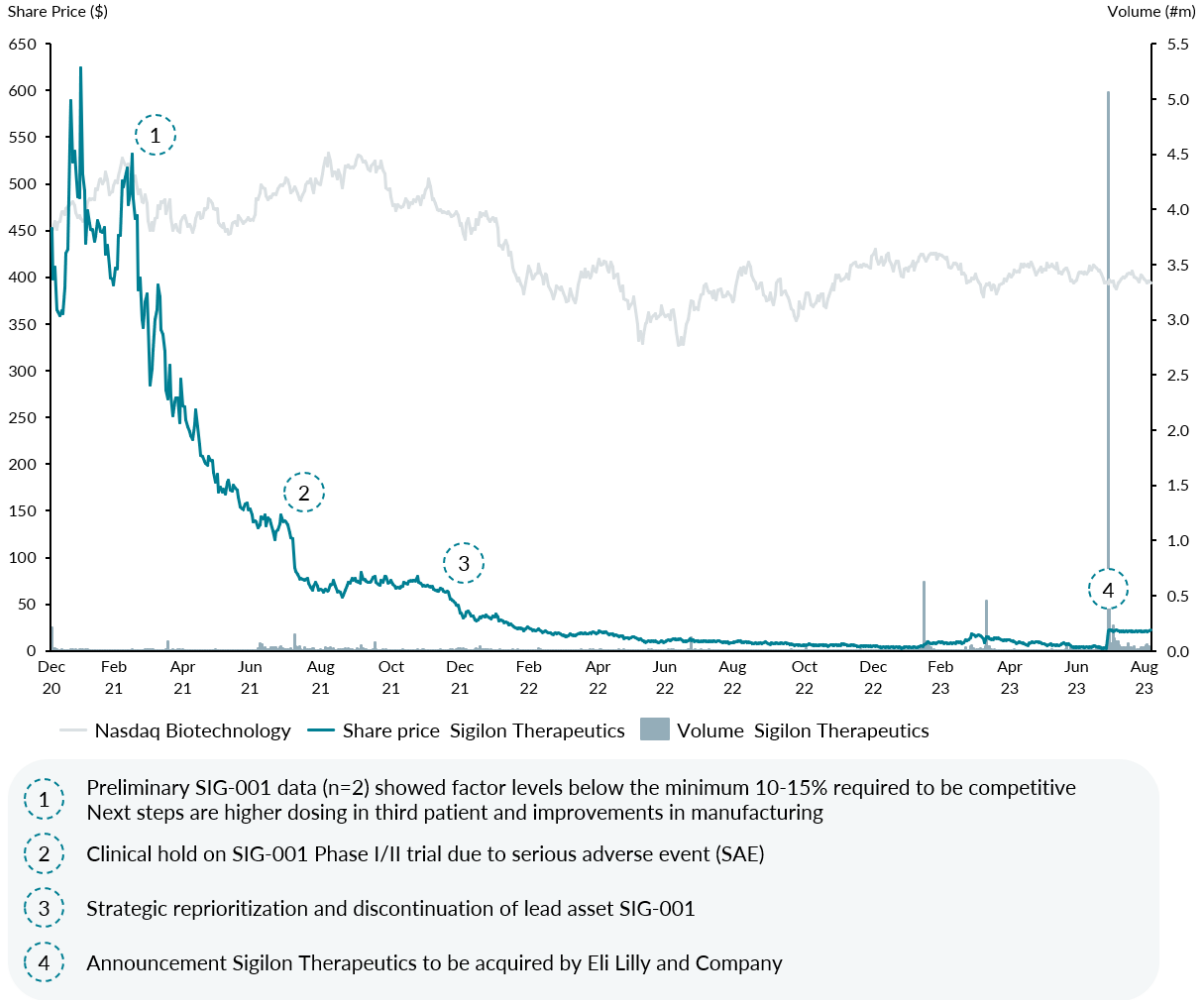

Exhibit 12 | Share price chart of Sigilon Therapeutics (NSDQ: SGTX) since its initial public offering (Refinitiv Eikon, n.d.). Several key moments in time are highlighted. *Nasdaq Biotechnology (NBI) is rebased to Sigilon Therapeutics' share price as per December 4, 2020 ($452.14); Share price of Sigilon Therapeutics is adjusted for stock splits.*

Insights & Reflections

Once it became clear that the Afibromer™-coated spheres did not possess the anticipated anti-fibrotic properties, Sigilon had to return to their pre-clinical research. By early 2023, only SIG-002 for type 1 diabetes remained under development in accordance with the obligations of the 2018 Lilly-Sigilon partnership agreement. Sigilon had transitioned from a promising, early-stage clinical company into a discovery-phase company running out of cash.

6.5 Rescue unfolds (2023)

It is early 2023, we are approaching the anticipated announcement of the Lilly-Sigilon acquisition on June 29, 2023. We have explored the events that led to the significant decline of Sigilon Therapeutics' share price –the clinical hold, the strategic reprioritization, and the dire financial position. Sigilon, once an up-and-coming biopharma company, has its back against the wall. We turn to the negotiations between Lilly and Sigilon leading up to the final offer.

The pre-negotiation phase

In the midst of its challenges, Sigilon Therapeutics found a potential lifeline in the form of Eli Lilly and Company. Yet, the path leading up to the actual merger negotiations was not without its obstacles. As early as December 2021, a member of Sigilon's board initiated a conversation with a representative of Lilly to explore 'potential strategic alternatives' (see Exhibit 13). While the specific strategic alternatives considered remain undisclosed, the most probable option appears to be the potential sale of Sigilon Therapeutics. Despite initial indications that Lilly had no interest in acquiring Sigilon, the narrative shifted in September 2022, when discussions intensified. During a regular catch-up call, Sigilon mentioned the exploration of strategic alternatives and its engagement with financial advisors, which prompted Lilly to suggest involving their business development team. The following meetings between Lazard and Lilly representatives laid the groundwork for discussions on potential transaction structures related to Sigilon's assets and R&D programs. Through a sequence of conversations, the two companies looked into varying deal structures, ultimately resulting in Lilly expressing their potential interest in a whole company acquisition on May 4, 2023. From there on, the actual negotiations between the two companies started (United States Securities and Exchange Commission, 2023a).

Date	Past contacts between Sigilon and Lilly
April 2, 2018	The Lilly-Sigilon agreement was signed. Following this agreement, Rogerio Vivaldi met regularly with representatives of Lilly to discuss the collaboration and Sigilon's strategy.
December 16, 2021	A member of Sigilon's board contacted a representative of Lilly to discuss the collaboration and potential strategic alternatives. Lilly's representative indicated that Lilly was currently not interested in acquiring Sigilon.
September 13, 2022	Following a regularly scheduled call, a representative of Lilly emailed Rogerio Vivaldi to suggest that he introduces Lazard to Lilly's business development team to discuss Sigilon's strategic process
September 14, 2022	Representatives of Lilly and Lazard held a meeting. Lilly's representatives indicated that Lilly was still not interested in an acquisition, but it remained open to discuss alternative transactions related to Sigilon's assets and programs.
September 19, 2022	A representative of Lilly explained to Rogerio Vivaldi that Lilly was not interested in acquiring Sigilon unless the transaction had only a small premium to Sigilon's trading price or the amount of cash on Sigilon's balance sheet.
October 28, 2022	Representatives of Lilly and Lazard discussed the valuation and structure of the transactions Sigilon was considering as well as the potential acquisition of Sigilon by Lilly
November 1, 2022	A representative of Lilly notified Rogerio Vivaldi that Lilly had decided not to participate in the strategic process at that time because, among other reasons, it was satisfied with the terms of the Lilly-Sigilon agreement of 2018.
December 5, 2022	A representative of Lilly requested Lazard for an update on the status of the strategic process.
April 28, 2023	A representative of Lilly indicated to Rogerio Vivaldi that Lilly may have an interest in acquiring Sigilon's assets, including the intellectual property and equipment, if Sigilon pursued a transaction with a counterparty that did not attribute value to Sigilon's assets, other than cash and its public listing
May 1, 2023	The representatives of Lilly and Lazard hat a meeting to discuss the potential benefits of a whole company acquisition relative to an asset acquisition. Lilly indicated that it was still not interested in acquiring Sigilon.
May 2, 2023	Rogerio Vivaldi emailed to a representative of Lilly reiterating the potential benefits of a whole company acquisition and providing additional information about Sigilon's financial position. Lilly responded that it would continue to evaluate both a whole company acquisition and an asset acquisition.
May 4, 2023	Representatives of Lilly expressed potential interest in a whole company acquisition.
May 7, 2023	Lilly provided an initial indication of interest.
May 12, 2023	Lilly submitted a revised version of the initial indication of interest.
May 24, 2023	Lilly submitted a second indication of interest.
May 30, 2023	Lilly submitted a best-and-final, third indication of interest.
June 27, 2023	Lilly's Chief Executive Officer reviewed and approved the Merger Agreement.

Exhibit 13 | Overview of past contacts between Sigilon and Lilly (adapted from United States Securities and Exchange Commission, 2023a). *Not exhaustive.*

The negotiations

On May 7, 2023, Lilly submitted an initial non-binding indication of interest to acquire Sigilon Therapeutics (United States Securities and Exchange Commission, 2023a). This initial proposal consisted of an upfront cash payment to cover Sigilon's net cash balance and a CVR component (see Exhibit 14). While the specifics of the CVR were still undefined at this point, Lilly's proposal intended to restructure the milestone payments that would have been paid under the 2018 Lilly-Sigilon partnership. The CVR component was included to make the proposal more attractive to Sigilon's shareholders.

Timing	Proceeds
Upfront payment	Net cash of the company (estimated to be ~$40 million) Minus transaction and integration expenses (estimated to be ~$7 million)
Future payment	A CVR component to be specified

Exhibit 14 | Initial indication of interest from Eli Lilly on May 7, 2023 (United States Securities and Exchange Commission, 2023a).

Following the initial indication of interest, Lilly and Lazard engaged in a conference call to discuss the details of the CVR component. After signing a Mutual Confidentiality Agreement, Lilly submitted a revised version of the initial indication of interest, specifying the CVR component (see Exhibit 15).

Timing	Proceeds
Upfront payment	Net cash of the company (estimated to be ~$40 million) Minus transaction and integration expenses (estimated to be ~$7 million)
Future payments	$10m upon first dosing of a Product in a Phase I clinical trial $50m upon first dosing of a Product in a Phase III clinical trial

Exhibit 15 | Revised initial indication of interest from Eli Lilly on May 12, 2023 (United States Securities and Exchange Commission, 2023a).

On May 17, Lilly and Lazard discussed the revised version of the initial indication of interest. Lazard told Lilly that they were not content with the value of the CVR proposal, which was significantly lower than the $415m in milestone payments outlined in the 2018 Lilly-Sigilon partnership (see Exhibit 5). In response, Lilly submitted a second indication of interest on May 24, 2023.

Timing	Proceeds
Upfront payment	Net cash of the company (estimated to be ~$40 million) Minus transaction and integration expenses (estimated to be ~$7 million) Plus $15 million

Exhibit 16 | Second indication of interest from Eli Lilly on May 24, 2023 (United States Securities and Exchange Commission, 2023a).

According to Lilly, the objective of this second indication of interest was to find a balance between the value attributed to an upfront cash payment that carries no risk, and the value of a substantially larger CVR payment, with a higher degree of risk. An added benefit of this payment structure was that it would require a single cash payment, thereby minimizing the administrative costs for Lilly.

Nevertheless, this offer failed to satisfy the shareholders. On May 26, 2023, Doug Cole from Flagship Pioneering engaged in a conference call with Lilly. The agenda revolved around the potential restructuring of the second indication of interest to reintroduce the CVR and to discuss its possible value. In addition, Doug Cole addressed the future of Sigilon under Lilly's ownership, taking into account aspects like talent retention. Following this conversation, Lilly would submit a best-and-final, third indication of interest. This proposal would contain an upfront payment based on Sigilon's cash position, and a CVR component that was higher than in the previous proposals.

Timing	Proceeds
Upfront payment	Net cash of the company (estimated to be ~$40 million) Minus transaction and integration expenses (estimated to be ~$7 million)
Future payments	$10m upon first dosing of a Product in a Phase I clinical trial $65m upon first dosing of a Product in a Phase III clinical trial $200m upon first regulatory approval of a Product

Exhibit 17 | Third indication of interest from Eli Lilly on May 30, 2023 (United States Securities and Exchange Commission, 2023a).

The third indication of interest managed to convince the selling shareholders. Lazard inquired about the possibility of including a CVR linked to Sigilon's other programs. However, Lilly was resolute in its decision not to incorporate any additional CVRs. On June 1, 2023, Sigilon presented a new version, which reflected Sigilon's cash position at closing and better estimates of the expenses. Additionally, it emphasized that all considerations would be directed exclusively to non-Lilly Sigilon stockholders. Finally, on June 9, 2023, both Lilly and Sigilon officially executed the third indication of interest. After conducting thorough due diligence and carefully drafting the merger agreement, Lilly's Chief Executive Officer reviewed and granted approval to the finalized merger agreement on June 27, 2023. Subsequently, on June 28, 2023, the merger agreement was officially executed (United States Securities and Exchange Commission, 2023a). In light of these events, it becomes evident that Lilly held a stronger negotiating position than Sigilon Therapeutics.

The final offer

After a long process tracing back to December 2021, Sigilon and Lilly published a joint press release on June 29, 2023, announcing the acquisition before the trading day started (Sigilon Therapeutics, 2023d). Lilly's final offer consisted of an upfront cash payment of $14.92 and a non-tradeable CVR. The upfront cash payment, totaling approximately $34.6m, essentially equals the cash on Sigilon's balance sheet after accounting for transaction and integration expenses. This implies that, effectively, Lilly will not be paying anything to acquire the (limited) tangible and intangible assets from Sigilon's shareholders. Based on the documented negotiations, it appears that the Supporting Stockholders, represented by Doug Cole from Flagship Pioneering, decided to embrace a certain degree of risk, in the hope to collect a more substantial profit through the CVR payments, rather than settling for a guaranteed, but relatively small payment of less than $6.50 per share (an aggregate of $15m) (see Exhibit 16). Should Lilly successfully reach the milestones within the specified time period, CVR holders stand to gain an additional $111.64 per share in cash: a calculated risk that Sigilon's shareholders were willing to take.

The CVR component of the Lilly-Sigilon acquisition is described in the Contingent Value Rights Agreement (United States Securities and Exchange Commission, 2023b). According to this agreement, three CVR payments will be triggered upon achieving specific milestones related to

the development and approval of a 'Product'. This 'Product' is an SLTx product candidate consisting of islet cells, i.e. cells that mimic or function as pancreatic islets of Langerhans, encapsulated by the SLTx encapsulation technology. The following three milestone payments are outlined in the Contingent Value Rights Agreement:

The **First Dosing Milestone Payment** of $4.06 in cash, without interest, per CVR, will be triggered when the first human patient is being dosed with a Product in a Phase I clinical trial before 12:00 a.m., Eastern Time on July 31, 2027 (United States Securities and Exchange Commission, 2023b).

The **First Registration Purposes Dosing Milestone Payment** of $26.39 in cash, without interest, per CVR, will be triggered when the first patient is being dosed with a Product in a Phase III trial before 12:00 a.m., Eastern Time on December 31, 2028 (United States Securities and Exchange Commission, 2023b).

The **Marketing Authorization Milestone Payment** of $81.19 in cash, without interest, per CVR, will be triggered when a Product receives marketing authorization in a) the United State, b) Japan, or c) three of France, the United Kingdom, Italy, Spain, and Germany, before 12:00 a.m., Eastern Time on December 31, 2031 (United States Securities and Exchange Commission, 2023b).

The Contingent Value Rights Agreement states that 'Lilly and its subsidiaries, licensees, and rights transferees, shall use Commercially Reasonable Efforts to achieve each milestone, provided that the use of Commercially Reasonable Efforts does not guarantee that Lilly will achieve any milestone by a specific date or at all' (United States Securities and Exchange Commission, 2023b). After the acquisition was finalized on August 14, 2023, Lilly and the former Sigilon employees joined forces to advance Sigilon's technology (Eli Lilly & Company, 2023c).

> *"We are excited to welcome our new colleagues from Sigilon to Lilly; together, we will strive to provide solutions for people living with type 1 diabetes that absolves them of constant disease management, and advance Sigilon's technology for patients."*
>
> *– Ruth Gimeno, Vice President Diabetes, Obesity, and Cardiometabolic Research at Lilly (August 14, 2023)*

6.6 Insights & reflections

At the beginning of this case study, two key questions emerged: How did Sigilon Therapeutics find itself in a situation where its stock price had dropped below the minimum listing requirements? And why did Sigilon's shareholders agree to be acquired by Lilly, receiving just $35m upfront, along with the prospect of a substantial $275m in potential CVR payments? Insights from diverse sources provided a comprehensive overview of the complex interplay between events and decisions that led to the Lilly-Sigilon acquisition.

Sigilon Therapeutics had a promising start, thanks to the groundbreaking SLTx technology that held the potential for major therapeutic advantages compared to other cell and gene therapies. With support from Eli Lilly through their partnership in 2018, Sigilon developed and expanded its pipeline rapidly**.** The growth reached its peak in 2020 with a highly successful Series B funding round and a subsequent IPO. However, adversity struck in 2021. First in-human studies revealed discouraging results: the SLTx encapsulation technology did not accomplish what was anticipated.

Contrary to expectations, the SLTx technology, which was believed to prevent an immune response against the encapsulated cells, instead triggered pericapsular fibrotic overgrowth.

Subsequently, the share price continued to decline. In 2022, Sigilon had to go back to the drawing board, restarting the pre-clinical studies to improve their existing technology. During this period, the company was losing money rapidly. By the second half of 2022, Sigilon began exploring several strategic options, suggesting that they were either seeking funding to keep the business running or putting themselves up for sale. In the end, long-lasting partner Lilly agreed to the idea of acquiring Sigilon as a whole. Lilly held a strong negotiating position, which ultimately influenced the acquisition's terms and conditions and negatively affected Sigilon's shareholders.

Sigilon Therapeutics was one of many emerging biopharma companies aspiring to achieve significant successes. Now, only a few questions remain: Can Lilly and Sigilon's former employees successfully develop encapsulated cell therapy for type 1 diabetes patients? Will they be able to reach the payment-triggering milestones before the deadline expires? And if not, will the Lilly-Sigilon acquisition result in litigation? Only time will tell.

7. Implications

The Investment Banking department at Van Lanschot Kempen is one of the leading players in the field of Life Sciences and Healthcare. Their Corporate Finance team continuously strives to stay on top of industry trends and to deliver specialized expertise to their clients. In the United States, one of the recent industry trends has been the growing use of CVRs in public biopharma M&A. Trends like this one, typically originate in the United States, gradually spread to the United Kingdom, and eventually make their way into the broader European market. Knowledge of emerging instruments such as CVRs is essential for staying competitive in the highly specialized field of financial advisory. Therefore, this study aimed to investigate the following questions: 1) What are the reasons behind the upward trend in the use of CVRs? 2) Why are CVRs more often incorporated in deal structures in the US than in Europe? 3) What are situations in which CVRs prove to be particularly valuable? 4) What does this emerging trend imply for financial advisers at Van Lanschot Kempen?

First, we will give a comprehensive answer to the first two questions by consolidating the insights from Chapters 4 and 5. Next, we will use the findings about trends in the broader biopharma M&A industry, to contextualize the observations from the case study. This will enable us to elaborate on the different situations in which a CVR might be useful. Finally, we will provide recommendations for financial advisers with regards to the emerging upward trend in the use of CVRs.

7.1 Understanding the rise of CVRs

The biopharma M&A industry has faced a substantial downturn throughout 2022 and into early 2023, with a decrease in both the number of deals and the overall value of transactions. Remarkably, while the day-to-day operations of biopharma companies have remained relatively unaffected, the M&A industry has been under considerable pressure, mainly due to a combination of macroeconomic and geopolitical challenges. These challenges include the impact of increasing interest rates, ongoing inflation, and economic uncertainty, as well as geopolitical tensions between the West and China, and the war in Ukraine. The rising cost of capital and overall market instability have led to a decrease in deal appetite, ultimately resulting in a decline in biopharma valuations. This has effectively shifted the landscape to what is often referred to as a buyer's market, offering favorable conditions for companies who are looking to acquire.

Nevertheless, the biopharma M&A industry is anticipated to take off in the last months of 2023 for a number of reasons. Despite the recent drop in valuations, emerging biopharma companies may soon find themselves under increasing pressure to explore the option of selling. This pressure is particularly pronounced for companies trading below cash or nearing the end of their cash runway, as they either need to raise capital or pursue an exit strategy. Adding to this, the route to the public markets has become more complicated for emerging biopharma companies, making an M&A exit more appealing. Furthermore, early investors in emerging biopharma firms who are eager to realize returns on their investments, may increasingly push for an exit strategy.

On the other hand, from a buyer’s perspective, the declining valuations within the biopharma sector could be a compelling reason to actively seek M&A opportunities. Moreover, large biopharma companies are facing a patent cliff, which necessitates the search for external innovation in order to sustain their long-term growth and competitiveness. Importantly, these companies have substantial cash reserves, enabling them to effectively fund these external innovation strategies. While these industry dynamics might propel biopharma M&A in the upcoming months, they have also resulted in substantial gaps between what sellers expect their assets or companies to be worth and what buyers are actually willing to pay. As a result, it is anticipated that there will be an increase in the number of deals involving a CVR. Through this

analysis, we have provided a solid foundation for comprehending the broader context in which CVRs are being employed and some of the factors driving their growing adoption.

Another important aspect contributing to the increasing use of CVRs in biopharma M&A is their suitability for the life sciences industry. Within the life sciences industry, business models often revolve around strategic partnerships with larger biopharma companies, which typically entail upfront payments and (pre-)clinical milestone payments similar to those found in a deal structure with CVRs in public M&A. Additionally, assessing the value of a biopharma company often relies on estimating the probability of success for certain milestones in the drug development process, e.g. initiation of a clinical trial or obtaining regulatory approval. When the seller and buyer have differing expectations regarding the likelihood of achieving these milestones, and thereby diverge in their valuations, an event-driven CVR can serve as a valuable mechanism for aligning their valuations.

While CVRs appear to be useful for bridging valuation gaps in the United States, their use in Europe remains rather limited. Several factors contribute to this difference. In the United States, people often adopt a more progressive approach to dealmaking and are more open to exploring creative solutions. Additionally, CVRs have a longer history and broader acceptance in the United States than in Europe. Conversely, the use of CVRs in Europe has been relatively limited, primarily due to the absence of established legal precedents. Nevertheless, it is important to recognize that the higher number of deals in the United States naturally results in a greater prevalence of CVRs compared to Europe. As mentioned before, trends typically originate in the United States and eventually make their way into the broader European market. So when American bidders, who are well-acquainted with this instrument, engage in acquisitions in Europe, they might choose to use it. Once a legal precedent is set, we anticipate that this trend will extend into Europe, as the CVR is just as useful in this region as it is in the United States.

So far, we have investigated the trends influencing the use of CVRs in the wider biopharma M&A industry. Yet, to gain a deeper understanding of the factors influencing the decision to include a CVR at the *company level*, a real-world case study was carried out.

7.2 The Lilly-Sigilon case study

A case study was conducted because the reason to include a CVR in the deal structure is shaped by a variety of factors that may not always be readily apparent. Therefore, these factors should be assessed on a case-by-case basis. The Lilly-Sigilon case study is particularly suitable because it unfolded during the current market conditions, allowing us to contextualize the observations with the previously discussed insights from Chapters 4 and 5. The fact that the CVR milestones have not been achieved yet, is not a cause for concern. The primary objective of this case study is to gain an understanding of the situations in which including a CVR might be the right course of action, not to evaluate what actions should be taken to prevent litigation. Moreover, what sets this case apart is that the deal structure involved a massive CVR compared to the upfront deal value. This indicates that the situation was not a simple disagreement about the valuation of a small aspect of the business, but rather a complex and multifaceted scenario.

Sigilon's promising business case

To fully understand what decisions and events led to the Lilly-Sigilon acquisition in 2023, we must evaluate how Sigilon's business evolved over time. In early 2021, at the peak of its existence, Sigilon Therapeutics had a strong business case. The company successfully employed an asset creation and out-licensing business model, which involved developing multiple pre-clinical assets using the SLTx technology platform, and then licensing them to large biopharma companies for

further development and commercialization. Several value drivers were positively affecting the company's valuation.

In theory, Sigilon's business case had the potential to generate large revenues in the future, while keeping costs to a minimum. Once approved, the proprietary and highly modular SLTx platform could be rapidly expanded into different disease areas, meaning that the company could tap into a sizeable market and generate substantial sales. In addition, if the SIG-002 asset would reach the market, the partnership with Lilly would ensure a dependable stream of cash inflows in the form of milestone payments and royalties. In terms of costs, Sigilon's 'off-the-shelf' platform was anticipated to create significant synergies in manufacturing, while providing an opportunity to leverage prior (pre-)clinical studies. Eventually, the COGS were expected to be significantly lower than competing cell and gene therapies. Moreover, the partnership enabled Sigilon to outsource the resource-intensive clinical trials to the more experienced Lilly, thereby avoiding investments in obtaining these capabilities.

During Sigilon's glory days, the company's potential return appeared to outweigh the associated risks. While the probabilities of a Phase I asset reaching the market are fairly low, Sigilon managed to raise substantial capital before releasing any clinical trial data. Undoubtedly fueled by the highly favorable market conditions, characterized by exceptional valuations, considerable investor interest, and high capital liquidity, Sigilon closed an upsized Series B financing round and a successful IPO. A few months into 2021, the initial Phase I/II results demonstrated that, although the therapy did not cause serious adverse events, it did not reach the required efficacy levels either. As a result, some investors lost interest, which led to a subsequent decline in the share price.

The results of the investigations into the clinical hold fundamentally changed Sigilon's business outlook and its valuation. In 2022, Sigilon found itself in a dire position for a number of reasons. To begin with, Sigilon had only few pre-clinical assets under development, which were overshadowed by the pericapsular fibrotic overgrowth observed in the Hemophilia A program. The company's meagre pipeline had a detrimental effect on the company's valuation and share price. Moreover, Sigilon may have experienced growing pressure from its major shareholder, Flagship Pioneering, to develop a strategy that would allow them to recuperate at least some of their investments. Lastly, the company was running out of cash and needed to raise capital in the near term. By the end of 2022, Sigilon had engaged Lazard as financial adviser to explore strategic alternatives. Given these circumstances, what were Sigilon's possible options?

Sigilon's strategic alternatives

Based on the analysis conducted in this report, Sigilon had five strategic alternatives. Given that Sigilon was a publicly traded company, it could try to raise capital by selling new shares to the public. However, as described in Chapter 4.2, follow-on transactions experienced a substantial decline in 2022. Moreover, Sigilon had a poor business case and its share price was in no condition to raise capital. Debt financing was not an option because the company had no prospects of generating revenues in the foreseeable future. Sigilon could have explored the possibility of finding a new partner to co-develop an asset with, and subsequently using the upfront payments to finance the business. However, in 2022, the company had few assets in their pipeline, and the clinical hold casted a shadow over these assets. This likely made the search for a new partner an impossible task. Clearly, one of the strategic alternatives was to sell the company. Based on the past contacts between Sigilon and Lilly (see Exhibit 13), this appears to be Sigilon's attempted course of action from September 2022 onwards, albeit with limited success. If no party were to acquire the company, Sigilon had only one option left: file for bankruptcy.

Lilly waited till there were no other options left before expressing their interest in a whole company acquisition. During the negotiations with Lilly, it was Doug Cole from Flagship Pioneering who successfully renegotiated a considerable CVR back into the deal structure. It is likely that he had made an assessment of risk and return, estimating that the option of substantial future profits outweighed a smaller, immediate payout. Lilly was willing to honor that request because, for them, this structure essentially allowed them to acquire Sigilon at no initial cost, while gaining access to a potentially promising, new treatment modality for type 1 diabetes. Ultimately, from Sigilon's perspective, the CVR was included in the deal structure because this was their only option to tap into the potential future value. In contrast, from Lilly's perspective, the CVR provided an opportunity to 'sweeten the deal' and to satisfy the shareholders.

7.3 The reasons behind CVRs

Generally, CVRs are a tool used to align the interests of two parties involved in public M&A negotiations. In this report, we have found that the decision to incorporate a CVR can arise from various motivations from both sides of the deal.

Reason 1: 'To bridge the valuation gap'.
Consider a scenario where two parties have reached an agreement on the valuation of 90% of a business, while strongly disagreeing on the remaining 10%. In this situation, due to asymmetric information, the sellers might believe that the technology they are developing has a higher chance of success, and therefore estimate the value of assets higher than the potential buyer. Here, a CVR could offer a solution 'to bridge the valuation gap'. This situation is more likely to occur under the current market conditions where sellers may still hold onto the high valuations from a year ago, while buyers base their offers on the current lower market values.

Reason 2: 'To mitigate risk'.
From the perspective of a buyer, a CVR can serve as a valuable tool to manage risk. For example, a seller might hold an optimistic view of their asset, while the buyer recognizes the potential risks associated with its clinical trials. In this case, the buyer may want 'to mitigate risk' by incorporating a CVR in the deal structure. Another example emerges during times of market uncertainty, when it becomes increasingly challenging to assess the impact of the evolving macroeconomic conditions on the valuation of the business. In such cases, there are two options. One can either wait until there is a clear outcome and a more precise understanding of the company's value, or proceed with the transaction. If the decision is made to move forward with the transaction, a combination of cash and a CVR can help to mitigate some of the risks.

Reason 3: 'To sweeten the deal'.
From the perspective of a buyer, a CVR can represent an opportunity to enhance the attractiveness of the deal for the sellers. To illustrate, consider the case of Steinhoff International where the company's management decided to incorporate a CVR into their offer. The banks had €10bn in debt outstanding, essentially allowing them to have a claim on all the remaining value within the company. As a result, there was nothing left to offer the shareholders, rendering their shares effectively worthless. A CVR was offered 'to sweeten the deal', allowing existing shareholders to potentially benefit if the company's assets were to recover in the coming years. Similarly, in the Lilly-Sigilon case, Lilly offered a CVR to appease Sigilon's shareholders.

Reason 4: 'Lack of alternative options'.
It is important to emphasize that CVRs may not always be advantageous for the seller. There are instances where sellers might have little choice but to accept CVRs, either because the overall deal

is exceptionally attractive or due to a lack of alternative options. To illustrate, consider the shareholders of Steinhoff, who were left with a poor negotiation position because the banks held a priority claim on the remaining value. Likewise, Sigilon's shareholders found themselves in a vulnerable negotiating position, with Lilly being their final resort, leaving them with no alternative but to accept the CVR.

These examples illustrate that the motivations for incorporating a CVR in the deal structure can differ between the selling and buying parties, and are frequently intertwined.

7.4 Conclusions & recommendations

As we emphasized at the beginning of this chapter, being well-informed about emerging financial instruments like CVRs is essential for financial advisors working in the highly specialized field of life sciences and healthcare M&A. Based on the findings of our research, we have strong indications that the use of CVRs in biopharma deal structures will continue to increase, driven by the current, pressing market conditions. Once a legal precedent is set, we foresee that this trend will expand into Europe. European financial advisers can benefit from having a CVR in their toolkit to address various challenges in dealmaking, such as bridging valuation gaps and mitigating risk. However, it is important to acknowledge that CVRs are employed only a few times per year, are typically a backup plan, and carry significant (litigation) risks.

Being proactive in monitoring industry shifts will allow professionals to make informed decisions when it comes to implementing CVRs, particularly in the European context where awareness and expertise in this area among financial and legal advisers may still be limited. Both buyers and sellers should ensure that their advisers have the essential expertise to effectively negotiate and execute the deal. For this reason, we have formulated three CVR-related recommendations for financial advisers.

1) Financial advisers are advised to either obtain expertise in life sciences licensing agreements or gain in-depth knowledge about the structure of CVRs. This includes understanding suitable milestone events (initiation/completion of trials, regulatory approval, and sales), the commercially reasonable efforts clause that a buyer needs to fulfil, as well as how to effectively monitor these efforts.
2) Financial advisers should invest in educating themselves on the intricacies of valuing a CVR, which is often the most complex part of a CVR deal. This valuation requires financial advisers to make informed assumptions about the probability of the milestone events, as well as well as determining the appropriate amount of the payment. Recommendations 1 and 2 combined, are essential for effective negotiations and optimal results for the client.
3) Financial advisers should collaborate with legal professionals who have a good understanding of the CVR structure and its applicability in the European context. This is recommended because incorporating CVRs into European transactions may come with specific legal and regulatory considerations.

7.5 Limitations

The case study approach is often associated with three notable limitations. First, it is criticized for its potential lack of scientific rigor, as it may lack systematic procedures and it is often hard to reproduce. However, in the context of this study, strict scientific standards are not essential. The primary objective is to gain a practical understanding of CVRs in real-world scenarios. Even if the

specific case under examination happens to be an outlier, the learnings extracted from it could still be valuable.

The second limitation relates to researcher bias. Since this case study was conducted by a single individual with their own unique perceptions and limited resources, there is a possibility that the results and conclusions may deviate from the truth. However, every effort has been made to maintain objectivity and provide a proper analysis.

The third limitation revolves around the external validity of case studies, which implies that the findings may not be readily applicable to other situations. Nevertheless, similar to the concern about scientific rigor, the aim here is not to draw generalizable causal conclusions. Instead, our goal is to offer valuable insights into this particular case, which can be informative for financial advisers seeking practical knowledge about this topic.

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10. Appendix

10.1 Interview questions legal professional

Introduction

- We hebben elkaar eerder ontmoet toen jij en jouw collega's een seminar gaven over CVRs op het kantoor van VLK. Tijdens dit seminar hebben jullie verteld dat jullie op dat moment bezig waren met de afrondingsfase van de herstructurering van Steinhoff International.
- Om te beginnen, zou je wat meer kunnen vertellen over jouw achtergrond? En wellicht ook over de herstructurering van Steinhoff International? Wat maakte deze zaak zo uniek?

European (legal) environment

- Tijdens het seminar heb ik begrepen dat het gebruik van CVR's in Europa relatief beperkt is, zeker in vergelijking met de Verenigde Staten. Wat zijn de redenen hiervoor?
    - Spelen bepaalde juridische of regelgevende factoren hierbij een rol?
    - Zijn er bepaalde landen binnen Europa waar CVR's vaker worden gebruikt of minder beperkt zijn? Zo ja, wat zijn de redenen voor deze verschillen tussen regio's?

- Er lijkt op dit moment een opwaartse trend te zijn in het gebruik van CVR's. Ben je het daarmee eens en zo ja, wat zijn de redenen hiervoor volgens jou?
- Denk je dat de huidige marktomstandigheden invloed hebben op het gebruik van CVR's in Europese deals?
    - Als dat het geval is, welke specifieke marktomstandigheden zouden dit effect veroorzaken?
    - En als dat het geval is, hoe beïnvloeden de huidige marktomstandigheden dan precies het gebruik van CVR's?
    - Waarom niet?

CVRs in practice

- Zijn er, volgens jou, bepaalde situaties of soorten deals waarvoor CVR's bijzonder geschikt zijn?
- Bij het opzetten van een deal met CVR's, wat zijn volgens jou de belangrijkste dingen waar je rekening mee moet houden?
- Stel dat een overname wordt uitgevoerd met behulp van een CVR, welk signaal denk je dat dat geeft aan zowel de aandeelhouders als de bredere markt?
    - Zegt dat iets over de betrokken bedrijven?

Voor we door gaan naar de case, zou je nog iets kwijt willen?

Case questions

- Wanneer je een casus als deze onder ogen krijgt, waar let je dan als eerste op? Welke juridische aspecten zijn dan van belang? Voorzie je problemen?
- Deze deal vond plaats tussen twee Amerikaanse bedrijven. Zou een soortgelijke deal kunnen plaatsvinden in Europa?
- Hoe zouden de clausules over beëindiging vanwege faillissement of serieuze schending, zoals in de overeenkomst tussen Eli Lilly en Sigilon Therapeutics uit 2018 staat, invloed kunnen hebben gehad op de CVR en de overnameovereenkomst?

- Welke rol spelen de huidige markttrends en -omstandigheden bij het vormgeven van de beslissing om een CVR op te nemen in de overnameovereenkomst tussen Eli Lilly en Sigilon Therapeutics?
- De CVR in dit geval is aanzienlijk groter dan de vooraf betaalde som en vormt een aanzienlijk deel van de totale dealwaarde. Welke factoren zouden zo'n structuur kunnen hebben beïnvloed?
- Welke juridische maatregelen zouden genomen kunnen worden om ervoor te zorgen dat de beoordeling van het behalen van mijlpalen eerlijk, nauwkeurig en zonder belangenconflicten verloopt?

10.2 Interview questions financial professional

1. In wat voor situaties komt volgens jou een CVR goed van pas?
2. Wat zijn volgens jou de grootste uitdagingen wat betreft een CVR in Europese context?
3. Jaap Geleijns noemde twee punten die ik wel interessant vond.
    a. Allereerst zei hij de waardering van een CVR vaak het moeilijkst is en dat dat vaak de reden is dat er geen CVRs gebruikt worden. Ben jij het daarmee eens?
        i. Zo ja, wat maakt het zo moeilijk?
        ii. Zo nee, waarom niet?
    b. Ten tweede noemde hij dat het veel mensen CVRs niet kennen, ook financiële adviseurs niet. Ben je het daarmee eens?