

Article

Building Technology Enabled Platform Companies in Biopharma – A Perspective on Early-Stage Value Creation from Millennium, Alnylam, Moderna, & Kymera

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ABSTRACT

This paper addresses the topic of building platform-based companies in biopharma. We provide a short literature review on the topic, followed by a discussion of financing growth of platform companies. This is followed by case studies on four pioneering biopharma companies that cover the era of the mid-1990s until today. These companies are all well recognized pioneers and have gone thru their life cycles from founding, to building portfolios of products, to acquisition. Our mini-case studies include Millennium Pharmaceuticals (now a unit of Takeda), Alnylam, Moderna, and Kymera.) These also cover different technology bases for their respective platforms that have emerged during the last two decades since the emergence of the genomics revolution.

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1.0 INTRODUCTION AND OBJECTIVE

DRUG DEVELOPMENT IS a long journey and the process by itself is actually a continuum of creating value while managing and reducing multiple risks. Since the industry inception with Cetus in 1971, and then the pivotal foundation of Genentech in 1976, followed by Amgen in 1980 the biotech paradigm has evolved significantly from creating startups, and funding the creation of well-established biotech companies, to getting the first product approved by the FDA – most often in partnership with a larger pharma company. Many business models have been described over time with regard to how to employ different business strategies at various development stages^{1,2}.

As a biotech entrepreneur, many crucial strategic subjects need be reviewed and considered, even before embarking on their company. These include the technology robustness, uniqueness and applicability, how the potential solution addresses the unmet clinical need, the competitive landscape, culture, regulatory hurdles, reimbursement, etc. We suggest that an essential consideration is to determine the type of company they shall choose. In other words, is this a single product company or, is there potential for creating an enabling technology platform company. This paper reviews four landmark technology platform companies created in the past two decades, and all of whom have made significant impact by exploiting a platform strategy. We explore how they established a sustainable value base in their early stage and over time pivoted their platform into a proprietary R&D driven biotech, and ultimately transformed into platform companies that have brought transformative technologies to market. Our objective is to provide the future biotech entrepreneurs (our intended audience) with some insights of strategic value creation in the early stages of technology platform – based companies. The landmark platforms selected in this paper are a genomics company applying world-class technology to drug

1 Gary Pfeffer (2020) Lawton Burns. 'The Biotechnology Sector: Therapeutics', *The Business of Healthcare Innovation* 3rd edition. Cambridge University Press. pp. 135–149.

2 Craig Shimasaki (2020) 'Understanding Biotechnology Business Models and Managing Risk', *Biotechnology Entrepreneurship* 2nd edition. AP. pp. 163–176.

discovery (Millennium – now a subsidiary of Takeda), RNA interference (Alnylam), mRNA (Moderna), and emerging protein degradation (Kymera). These companies have demonstrated their abilities to innovate around an emerging and transformative technology to build platforms. The science, platform, culture, and leadership, are all absolutely critical in the process of capturing the value creation; however, that is not the theme of this paper. We focus on the elements of business model development that is required to build a platform company – beyond the technology itself.

2.0 TAXONOMY AND DEFINITION

Before we review those landmark companies, it would be important to clarify some key definitions and concepts associated with platform companies and understand how they create value. Platforms have been described in many books and articles, but to some extent conflicts and questions still exist.

2.1 ARE YOU A TECHNOLOGY PLATFORM COMPANY? AND WHICH TYPE?

Before we decide if we can build a platform company or not, we must define what constitutes a platform company. It is interesting to notice the differences discussed in two, recent biotechnology books. Millennium Pharmaceuticals was categorized as a subscription business model by Shimasaki, while Pfeffer defined it as a technology platform company¹⁻². Why does this difference exist? Lanza illuminated the criteria with some key questions that a successful platform company needs to answer³: 1) whether the technology is broadly applicable to address an industry wide problem, 2) whether the technology provides an alternative to existing processes, and, 3) whether the technology is scalable and offers greater efficiency. Three consecutive yes answers would lead to technology platform company, and Millennium is fully meets these criteria. However, a more instructive question is how to subcategorize the platform company, which probably results in the differences between Shimasaki and Pfeffer. I believe that Steven Holtzman addressed it perspicuously⁴. According to his taxonomy, there are two types of platform companies; product (therapeu-

tic modality) platform companies, and insight platform companies, and the latter includes two subtypes (pathway and target driven, and biology driven). The perception confusion associated with Millennium was that the company did use the service and subscription mode in the initial stage to generate revenues and advance the platform, however, it fully merits a target and pathway – insight driven platform company according to Holtzman (Genus 2 Species A). All the other three companies founded after 2000 and described in this paper actually are product platform companies (Genus 1) in his typology.⁴

To further illuminate the role of the platform in creating and sustaining value and competitive advantage, we highlight some of the recent work published by Boni in this journal and used to screen early stage companies, c. f. “Evolution of the Screening Metaphor: Project, Product, or Platform (JCB, Vol. 24, No. 4, pp 7–13 (2019). This article is a lead article in a special issue titled “Boot Camp 2.0” and used at each annual BIO Entrepreneurship Boot Camp (to assist emerging bio-entrepreneurs to build their potential companies). We include here some materials taken from that paper with permission of the author and the publisher:

“Projects are best pursued with commercial partners via licensing arrangements. Products may be pursued using a research and development company business model. Platform is intended to signify creation and growth of a lasting, scalable organization intended to develop and bring multiple disruptive or transformative innovations to market. Which path to the marketplace is appropriate, or even possible will depend on a number of factors. These include: the magnitude of value being created for the market; the competitive set; and, the uniqueness of the solution and its sustainable, competitive advantage that can be created. It is also necessary to determine whether the value captured by the business model that may be constructed could generate sufficient profitability to balance the commercialization risks, while meeting the goals and objectives of the founders, investors and partners over an appropriate time line.”

“One definition of “Platform” is the common foundation (or, technological) base from which one can create a family of products (and services), while targeting different customer segments. e. g. multiple disease states. Platforms are incorporated into business models

3 Lanza, G. Building today's platform company. Bioent (2009). <https://doi.org/10.1038/bioe.2009.6>

4 Steven Holtzman, Early-Stage Biotech Value Creation: The Roles of Equity and Partnerships. [http://](http://leadershipandbiotechnology.blogspot.com/2018/08/early-stage-biotech-value-creation_15.html)

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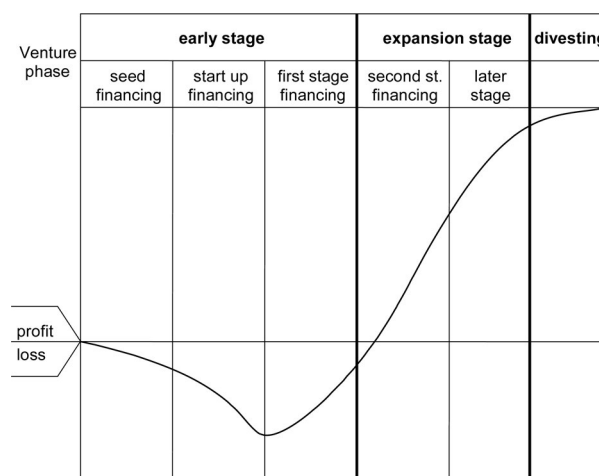


Figure 1: Typical Development phases of high growth companies
Source: Leleux IMD Case⁵

with the potential to create, deliver, and capture more value than a single product or service, and more importantly sustainably. They can also be used to allow multiple parties (“market sides”) to transact across the platform. “A multi-sided platform that connects partners, users and payers can create more value for all than just the entity that creates the platform” (a paraphrase of a Bill Gates quote).⁵

“The platform and its supporting ecosystem and network may be used to build and sustain a market leadership position vs. a single product with a much less powerful network. However, the early-stage company may start from a single product; then grow and dominate multiple market segments by developing a supporting ecosystem and network. Alternately, the organization can start with the vision of creating an industry leading platform, and use the entry product as a step in that direction. However, and depending on the industry and competitive landscape, it may be necessary for the early stage company to join existing networks of power players to provide complementary products or services. In today’s innovation landscape, platforms are most often thought of in the context of information technology (IT). However, the concept of a platform has been around for years and evidenced in the product pipeline/portfolio approach taken in the biopharma industry”.

2.2 BIOTECH VALUATION STAGE

Biotech companies face the need for valuation at various development stages. Leleux described that the possible

stages of a high-growth company that include: Seed stage (conceptualizing); Start-up stage (launching); First stage (Developing), Second stage (Accelerating Growth); Later stage (Restructuring for Value Added); and, Exit stage⁵.

It is essential to position a technology platform company at different stages because each would reflect specific risks attached to the safety, efficacy, competition, regulation, demand, etc. The amount of money raised at each crucial step needs to be justifiable and requires a careful and thorough analysis and rationalization, that will impact the future valuation estimations significantly. An early stage company must carefully evaluate what share they would have to cede to the investors in exchange for the investment, where to allocate its capital, and which project they should push forward to reduce risk and to ultimately achieve higher valuation associated with risk reduction.

In any finance textbook, value is typically defined as the expected future free cash flows discounted at the opportunity cost of capital. Although a variety of valuation methods can be considered, the discounted cash flow approach (DCF) are widely used with the focus on projecting appropriate discount rate and expected cash flow, particularly in the non-listed company.⁵ The adjustment of DCF can be roughly based upon the management, quality and uniqueness of the science, market potential, however, the market value could be primarily driven by expectation, i.e. the hope of realized earning potentials from approved drugs. As drug development is a long process and its value creation could take more than a decade to be captured, it is indeed the non-financial indicators that are key to valuation of a biotech

5 Benoit Leleux, Victoria Kemanian, Atul Pahwa, and Katrin Hacki. Venture Valuation AG: The Genedata Assignment. IMD Case: IMD251

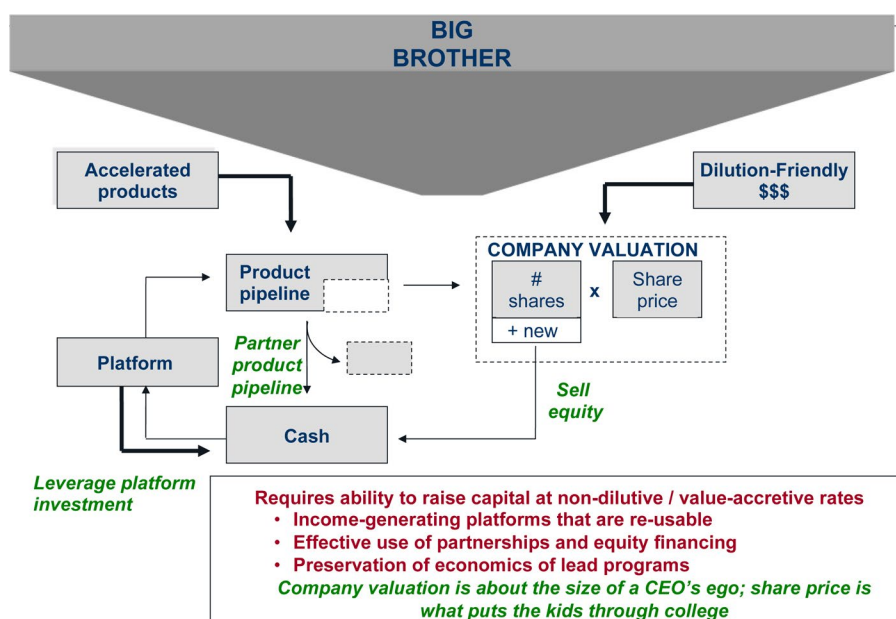


Figure 2: Biotech Value Creation Cycle (Source: Steve Holtzman Blog⁴)

company, which may include commencement and completion of milestone trials at different phases, approval of IND, strategic alliance (including marketing, R&D, and manufacturing, etc.), and product launch⁶. Compared with other measurable non-financial indicators, given high inherent risk of drug development, the intense competition in the drug marketplace, forming alliances and partnerships is essential to a platform company's valuation and boost the value creation cycle given its positive impact on investor's risk reduction and pipeline need, and more importantly to meet and exceed the investor's expectation and reinforce their confidence to attain the expected cash flow due to breakthrough discoveries that stemmed from the platform to address the desperately unmet need.

2.3 BIOTECH VALUE CREATION CYCLE

It is indeed a long journey before a biotech company can produce any revenue from product sales, therefore the value to be promoted to the investors is subject to discussion and rationalization amongst the parties. This would include the value at present, which could be technology insight, product potential to a partner company, including the value of perceived futures thru marketing/profit sharing, etc. Therefore, as Holtzman described, biotech value creation is not about the size or market capital, but predominantly

about share price appreciation. The focus of the size of market capital by absorbing too much dilution early would compromise the stakeholder's value. Therefore, when sourcing value accretive capital, any alliances and partnerships need be vigilantly balanced in a manner not to give away the major parcels of future value creation⁴.

In the next section, by observing some strategic value creation implementation process in a few paradigm platform companies particularly in their early stages, we would hope to reveal some success secrets during their value creation cycle.

3.0 PLATFORM COMPANY IN BIOTECH – MONOCLONAL ANTIBODIES (MAB) (LATE 1970S TO 1980S)

The discovery of monoclonal antibodies has defined the modern history of biomedicine. In 1983, based on a number of animal studies, the pioneers in mAb believed that a new era of cancer treatment would begin soon. In the following year, the landmark Nobel Prize was awarded to Georges Köhler and César Milstein. In 1996, Rituximab and trastuzumab were approved by the FDA as the first and second therapeutic mAb based cancer treatments⁷. It is worth noting that the first generation of therapeutic

6 McConomy, Bruce & Xu, Bixia. (2004). Value creation in the biotechnology industry. CMA Management. 29–31

7 Robert Oldham and Robert Dillman. Monoclonal Antibodies in Cancer Therapy: 25 Years of Progress. Journal of Clinical Oncology 2008 26:11, 1774–1777

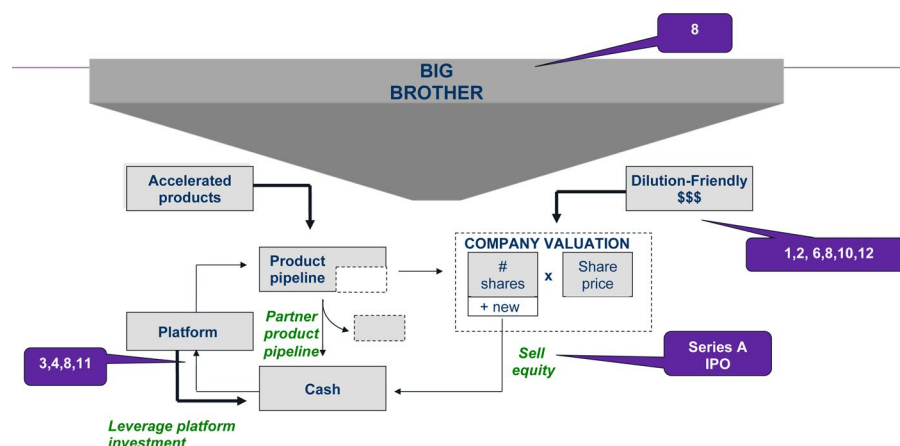


Figure 3: Biotech Early Stage Value Creation Cycle: Millennium Snapshot

modality platform companies such as Genentech were founded with different financing mechanisms from most of what we will discuss in 1990s and later, therefore, their strategic value creation will not be discussed in this paper.

3.1 MILLENNIUM PHARMACEUTICALS – VALUE CREATION VIA STRATEGIC ALLIANCES (1990s)

Millennium Pharmaceuticals, Inc. was founded in Cambridge, Massachusetts in 1993. Started as a technology platform company with \$8.5 million initial VC funding, it went public in 1996 and became one of the most successful biotech companies in the 1990s. It was managed and transformed into a fully integrated biopharma firm in early 2000s prior to being acquired by Takeda pharmaceutical in 2008 at \$8.8 billion.

Partnering with big pharmaceutical companies was fundamental to the growth of Millennium in its early stage. By leveraging the timing of the Human Genome Project, enthusiasm, and leadership, they controlled a significant early slice of the genomics pie. The company crafted a series of breakthrough strategic alliances with 8 of the 10 largest pharmaceutical companies in five years after its commencement; including a history of discovery alliances worth \$465 million agreement with Bayer, which also sped up their growth through aggressive acquisition strategy to secure their platform advancement, and made the company's market capitalization exceed \$4 billion by the end of 1999.

From the very start, the company decided to generate reliable revenue streams very early on. The management team scrutinized various failures of other small biotech firms, which were largely attributed to having narrow platforms, selling off product rights too soon,

huge sinking cost of development, and framed a clear strategy to build up a comprehensive technology “platform” that would empower them to develop and sell some of their assets, such as drug targets and later drug leads, to big pharms with hunger for new drug candidates, while preserving the capability to keep a good amount for the firm and retain ownership and IP for further development. Under this strategy, an array of proprietary technologies in the discovery chain, such as proteomics, bioinformatics, high-throughput screening, synthetic chemistry, cheminformatic, as well as molecular biology were assembled and merged into a state of the art “technology platforms.” Partnering with big pharmaceutical companies was a core step in CEO Mark Levin’s roadmap. A typical alliance agreement would include that pharmaceutical partner pay Millennium an upfront fee, and milestone payments when a predefined research milestone was achieved and take responsibility for potential downstream drug development and commercialization. The series of alliances and collected about \$2 billion in a few years and helped them strengthen technology platform and cultivate its capability of identifying its own drug leads to a variety of therapeutic areas^{8,9}.

The Table 1 below provided a snapshot of its deal distribution in the value creation cycle. As described in Section 2.1, Millennium was a novel and science insight driven platform company, and the value creation cycle illuminated that product in-incensing is less likely to feature in the value creation cycle. However, their relentless

8 Stefan Thomke. Millennium Pharmaceuticals, Inc. (A) Harvard Business School Case Number: 9-600-038 Rev: August 27, 2001

9 Julie Wulf, Scott Waggoner. Organization and Strategy at Millennium (A) Harvard Business School Case Number: 9-710-415 Rev: April 26, 2010

Table 1: Millennium selected early stage alliances (Source^{1,2})

Date	Deal #	Deal Type/Partner	Value(m)	Terms	Role of Millennium
1994	1	Hoffmann-La Roche	\$70	Equity investment and fees from partner	Gene/target research focus on Obesity, Type II diabetes
1995	2	Eli Lilly I	\$50	Equity investment and fees from partner	Focus on Atherosclerosis & Oncology
1996	3	Astra AB	\$60	Up-front Licensing Fees from partner	Focus on Inflammatory respiratory diseases
		Eli Lilly II	\$30	Up-front Licensing Fees from partner	Extension of previous deal
1997	4	AHP (Wyeth-Ayerst)	\$90	Up-front Licensing Fee from partner	Focus on General Nervous System disorders
	5	ChemGenics	\$90	Acquisition	Acquisition of lead research capability
	6	Eli Lilly III	\$20	Equity investment and milestone fees from partner	Extension of previous deal
	7	Monsanto	\$218	Fees from partner	Technology transfer to partner
1998	8	Bayer	\$465	Equity investment and Up-front Licensing fees from partner; ownership of targets not retained by Bayer	Gene/target research: Cardiovascular, Oncology, Osteoporosis, Liver fibrosis, hematology, viral infections. 225 targets over 5 y period
1999	9	LeukoSite	\$750	Acquisition	Acquisition of lead research capabilities, product development pipeline, and near-market products
	10	Becton Dickinson	\$68	Equity investment and fees from partner	Gene/target research
	11	Bristol-Myers Squibb	\$32	Fees from partner	Gene/target research
2000	12	Aventis	\$450	Equity investment and fees from partner; 50-50 ownership of end products	Full codevelopment of drug;cocommercialization in North America
	13	Cambridge Discovery Chemistry	\$50	Acquisition	Acquisition of chemistry capability
2001	14	Abbott Laboratories	\$250	Equity investment and fees from partner; 50-50 ownership of end products	Full codevelopment of drug;cocommercialization

1 <https://hbr.org/2001/06/mastering-the-value-chain-an-interview-with-mark-levin-of-millennium-pharmaceuticals>

2 Michael Watkins and Sarah Matthews, Strategic Deal-making at Millennium Pharmaceutical, HBS Case No. 800-032.

effort of consolidating their platform capabilities helped them secure competitiveness within a short period of time, and the massive non-dilutive investment from big pharma partners had supported their sustainable growth and allowed them to pivot and transform later. As seen in its early stage value creation cycle (Figure 4), their first-mover advantage, the genomics timing, groundbreaking platform nature, the charismatic leadership, as well as aggressive and savvy capital raising had helped them with rapid and remarkable value creation in

the early stage, thus impacted the company's valuation significantly.

3.2 ALNYLAM PHARMACEUTICALS – VALUE CREATION FROM THE IP ESTATE (2000s)

Alnylam Pharmaceuticals, Inc. was founded in Cambridge, Massachusetts in 2002 based on the RNA

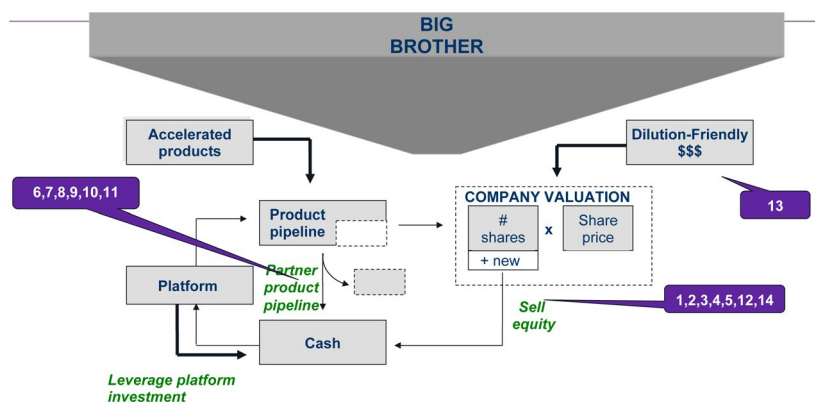


Figure 4: Biotech Early Stage Value Creation Cycle: Alnylam Snapshot

Table 2: Alnylam selected early stage alliances (Source^{13,1,2,3})

Date	Deal #	Deal type/Partner	Value(m)	Terms	Business Status/Role of Alnylam
2002.7	1	Series A	\$2	Venture Funding	Product Development
2002.8	2	Series B	\$15.5	Venture Funding	Generating Revenue
Undefined	3	Series C	\$17.5	Venture Funding	Generating Revenue
2004.3	4	Series D	\$30	Venture Funding	Generating Revenue
2004.5	5	IPO	\$30	Public Investment	Generating Revenue
2005.9	6	PIPE, Novartis	\$56.8	Strategic Alliance	Joint discovery of new RNAi therapeutics
2006.10	7	PIPE, Multiple VCs	\$24.6	Venture Funding	Generating Revenue
2007.8	8	PIPE, Roche	\$331	Strategic Alliance	Providing non-exclusive licenses on RNAi therapeutics
2008.4	9	GSK	\$600	Strategic Alliance	Via Regulus, a JV with ISIS, receive milestone payments for each of the four microRNA-targeted therapeutics
2008.5	10	PIPE, Takeda	\$1000	Strategic Alliance	Providing non-exclusive access to RNAi therapeutics in the fields of Oncology and metabolic disease
2010.6	11	Sanofi	Up to \$750	Strategic Alliance	Via Regulus, a JV with ISIS, receive milestone payments
2012.2	12	2PO	\$80.63	Public Investment	Generating Revenue
2014.2	13	PIPE, Genzyme/Sanofi	\$1,500.00	12% stake of Alnylam	Acquired Assets of Sirna Therapeutics
2015.1	14	2PO	\$432.00	Public Investment	Generating Revenue
2020.4	15	PIPE, Blackstone	\$100	Private Equity	Generating Revenue

1 Pitchbook: Alnylam Pharmaceutical

2 Pitchbook: Regulus Therapeutics

3 http://archive.boston.com/business/healthcare/articles/2010/06/28/regulus_makes_750m_deal_with_sanofi_aventis/

interference (RNAi) technology. Starting from \$2 million series A funding, it went public in less than two years and was one of the most high-profile therapeutic platform driven biotech companies in the early 2000s. In 2018, the FDA and European EMA approved their first-ever RNAi therapeutic ONPATRO (patisiran). In 2019, the FDA approved the second product, GIVLAARI (givosiran). At present, their RNAi driven pipeline includes three programs in late-stage clinical development and multiple programs in early-stage clinical development¹⁰.

The RNAi harnesses the technical viability to silence disease-causing genes at the RNA level before translation into protein occurs and the science began to materialize in 2001 when Tom Tuschl discovered the siRNA structure and was able to put the RNA into human cells to show ability to silence genes. People began to consider it a ground-changing technology with potentials for an entirely new therapeutic paradigm on treating many genetically based diseases by targeting a specific gene and silencing it. Alnylam was founded accordingly with aim to be the first mover when RNAi was still far from certain, and the founders all understood it would be a long journey to turn the technology into a therapeutic, and before that enormous investments would be needed.

They had a very explicit strategy at the beginning to consolidate the intellectual property and assemble a patent portfolio (the “patent estate”) all together so that anyone who anticipated therapeutic use of RNAi would have to license from them. After thoroughly reviewing the RNAi patent landscape, they identified eight frontier or associate patents in RNAi and negotiated all these different license grants, in agreements with academic institutions where those licenses were being held and secured either ownership or freedom to practice if without full control. By consolidating IP in this manner, they enjoyed pretty much non-competitive benefits, and were able to enhance their value creation by licensing the portfolio selectively and to raise sufficient non-dilutive funding capital from pharma partnerships. One of Alnylam’s earliest licensing deals, as an example, was with Novartis in 2005 to target discovering, developing, and commercializing RNAi therapeutics for a defined number of gene targets exclusively selected by Novartis. In July 2007, Alnylam got one of its biggest licensing deals with Roche, providing a non-exclusive license to Alnylam’s technology platform for developing RNAi therapeutics. The partnerships with big brothers funneled the money back into R&D to develop the necessary delivery mechanisms for RNAi and supported their ability to develop their own pipeline so as to avoid raising capital from more expensive capital markets. They also provided Alnylam with some grant-back licenses to discoveries from

licensees as well as access to other IP platforms from the partners. Licensing therefore worked as a hedge for its own research program and enabled Alnylam to cherry-pick other partners’ successful programs and potentially acquire partial ownership. Within 8 years, they raised \$950 million, in which only \$250 million was in the form of equity to venture capitalists or to the public markets and more than \$700 million came from non-dilutive licensing fee (IP estate), which significantly, although indirectly raised their appreciation over the time¹¹.

As illustrated in its early stage value creation cycle (Figure 4), their first-mover advantage, and ground-breaking product platform nature had driven their progressive value creation in the early stage using balanced partnerships and equity deals, and indirectly impact the company’s valuation. After 17 years since inception, their valuation had increased significantly attributing to the concept turning into products proved by the FDA.

3.3 MODERNA (2010s) – VALUE CREATION BEFORE COVID-19 VACCINE

Moderna, Inc. was founded in Cambridge, Massachusetts in 2010. They are pioneering their industry’s leadership based on a messenger RNA or mRNA technology platform, the infrastructure to accelerate drug discovery and early development. Their pipeline includes development candidates for mRNA-based vaccines and therapies spanning several therapeutic areas, and currently multiple clinical trials are underway, and its vaccine candidates has aggressively progressed through the clinic, and recently given vaccine approval for the Covid-19 pandemic. In December 2018, Moderna achieved the largest biotech IPO in history, raising US\$600 million for 8% of its share since inception¹². As of Aug 2020, Moderna was valued at \$25 billion, and none of its mRNA molecules had yet to enter into large clinical trials.

The concept of mRNA-based therapy is that by injecting mRNA therapeutics to the patient’s cells with the genetic code from DNA could get used again, the patient would be able to perform its protein producing function to cure the relevant diseases. Since its start as a private company, Moderna mostly performed in stealth mode with little disclosure of its research. However, they

10 <https://www.alnylam.com/>

11 Willy Shih, Sen Chai. Alnylam Pharmaceutical: Building Value from the IP Estate. HBS Case. Case number: 9-611-009. Rev July 15, 2013

12 <https://fortune.com/2018/12/08/moderna-ipo-biotech-future/>

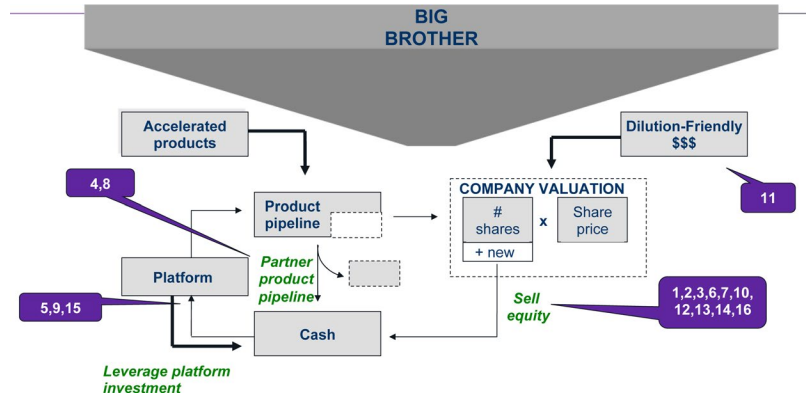


Figure 5: Biotech Early Stage Value Creation Cycle: Moderna Snapshot

Table 3: Moderna selected early stage alliances (Source^{1,2})

Date	Deal #	Deal type/Partner	Value(m)	Terms	Business Status/Role of Moderna
2010.10	1	Series A	\$2.1	Venture Funding	Generating Revenue
2011.12	2	Series B	\$9.2	Venture Funding	Generating Revenue
2012.12	3	Series C	\$27.6	Venture Funding	Generating Revenue
2013.3	4	AstraZeneca	\$240	Strategic Alliance	Exclusive access to select any target of tis choice in cardiometabolic diseases
2013.10	5	Grant, DARPA	\$24.6	Grant Funding	Generating Revenue
2014.1	6	Series D	\$135	Venture Funding	Generating Revenue
2015.1	7	Series E	\$450	Venture Funding	Generating Revenue
2016.7	8	Vertex	up to \$275	Strategic Alliance	milestones plus royalty for CF mRNAi therapeutics
2007.8	9	Grant, Bill &Melinda, BARDA, DARPA	\$331	Grant Funding	Generating Revenue, Supporting FIH study
2016.9	10	Series F	\$474	Venture Funding	Generating Revenue
2016.10	11	Debt, CIT group	\$1,340.00	Debt	Generating Revenue
2018.2	12	Series G	\$500	Venture Funding	Generating Revenue
2018.5	13	Series H	\$125	Venture Funding	Generating Revenue
2018.12	14	IPO	\$604.35	Public Investment	Generating Revenue
2020.4	15	Grant from Biomedical Advanced Research and Development Authority	\$483	Grant funding	Accelerating mRNA vaccine candidate against covid-19
2020.5	16	2PO	\$1,340.00	Public Investment	Generating Revenue

1 Pitchbook: Moderna Inc.

2 <https://www.fiercebiotech.com/biotech/vertex-moderna-pair-to-create-mrna-cystic-fibrosis-treatment>

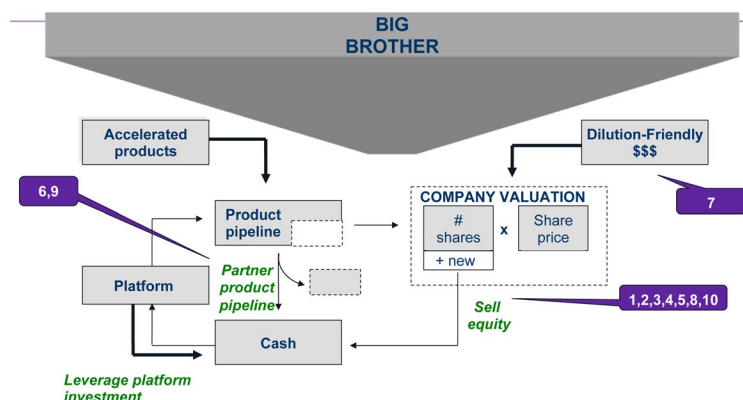


Figure 6: Biotech Early Stage Value Creation Cycle: Kymera Snapshot

quickly built strategic relationships with AstraZeneca, Merck and Vertex Pharmaceuticals, as well as the Defense Advanced Research Projects Agency (DARPA), the Biomedical Advanced Research and Development Authority (BARDA), and the Bill & Melinda Gates Foundation as they are passionate for the potential of its mRNA therapeutics, which could apply to a wide range of diseases from cancer to rare genetic conditions. As an example, in 2013, Moderna and AstraZeneca sealed a five-year exclusive option agreement to discover, develop, and commercialize mRNA for treatments in the areas of cardiovascular, metabolic and renal diseases, and selected targets for cancer. The agreement included a \$240 million upfront payment to Moderna and is considered “one of the largest ever initial payments in a pharmaceutical industry licensing deal that does not involve a drug already being tested in clinical trials”¹³.

As illustrated in its early stage value creation cycle (Figure 5), their initial investment via public investment is heavy. However, driven by the first-mover advantage, Moderna could raise massive non-equity capital in the early stage to complement its venture financing, and the curve at early stage (Figure 1) demonstrated the trend of steep value increasing curve even during expansion stage.

3.4 KYMERA – PROTEIN DEGRADER PLATFORM ON THE HORIZON (2020s)

Kymera Therapeutics, Inc. was founded in Cambridge, Massachusetts in 2017. Launching from stealth mode as an Atlas Venture backed incubator, Kymera is at the forefront of protein degradation R&D, with many other

pioneers such as C4 Therapeutics, Arvinas and Nurix. Kymera has marched forward steadily since then and completed an IPO on August 2020 with a \$173.7 million raise. The biotech is focusing research on a serial of lead programs designed to degrade IRAK4, IRAKIMiD and STAT3, respectively. IRAK4 was the star of the Sanofi alliance¹⁴.

Targeted protein degradation, as an emerging therapeutic modality, is dramatically progressing with massive investment in recent years. As part of cellular processes, proteins are specifically recruited to E3 ubiquitin ligases and tagged for destruction with chains of ubiquitin. Compared to inhibition strategies, degradation offers numerous advantages, including the chance for removal of the target protein and consequent ablation of all associated functions. The unique properties of degraders provide opportunities for widely differentiated therapeutics, as well as the chance to tackle pathologies driven targets that were previously considered undruggable^{15,16}.

According to the definition of technology platform in Section 2.1, indeed, this targeted protein degradation can broadly address industry’s problem of shortage in druggable targets, and technology provides an alternative to existing small molecule inhibitors, and technology is very scalable and offer greater efficiency. Although in the early stage, protein degradation technology has

13 <https://www.nytimes.com/2013/03/21/business/astrazeneca-to-pay-240-million-to-moderna-therapeutics.html>

14 https://www.contractpharma.com/contents/view_breaking-news/2020-07-09/kymera-sanofi-enter-multi-program-strategic-alliance/

15 Chamberlain, P.P., Hamann, L.G. Development of targeted protein degradation therapeutics. *Nat Chem Biol* 15, 937–944 (2019).

16 Mayor-Ruiz, C., and Winter, G.E. (2019). Identification and characterization of cancer vulnerabilities via targeted protein degradation. *Drug Discov. Today. Technol.* 31, 81–90.

Table 4: Kymera selected early stage alliances (Source^{1,2,3})

Date	Deal #	Deal type/Partner	Value(m)	Terms	Business Status/ Role of Kymera
N/A	1	Seed round	\$3	Venture Funding	Startup
N/A	2	Accelerator/Incubator	\$3	Venture Funding	Startup
N/A	3	Accelerator/Incubator	\$3	Venture Funding	Startup
2017.10	4	Series A, led by Atlas	\$30	Venture Funding	Generating Revenue
2018.11	5	Series B	\$65	Venture Funding	Generating Revenue
2019.5	6	Vertex (Series B1)	\$70	Strategic Alliance	Upfront to discover protein degrader drugs
2019.10	7	Debt from Multiple Debtors	\$13.85	Debt Financing	Generating revenue
2020.3	8	Series C	\$105.29	Venture Funding	Generating revenue
2020.7	9	Sanofi	\$150	Strategic Alliance	Upfront to discover protein degrader drugs
2020.8	10	IPO	\$173.7	Public Investment	Generating Revenue

1 Pitchbook: Kymera Therapeutics

2 <https://www.fiercebiotech.com/biotech/vertex-pays-kymera-70m-upfront-to-discover-protein-degradation-drugs>

3 <https://www.fiercebiotech.com/biotech/sanofi-pays-150m-upfront-2b-biobucks-to-tap-protein-degrader-biotech-kymera>

become an emerging breakthrough therapeutic modality, and Kymera, as one of the players, are working diligently to solidify its proprietary platform, which is likely to be continually validated from the high-value strategic partnerships with big brothers/partners, like Vertex and Sanofi. As illustrated in its early-stage value creation cycle (Figure 6), their value is driven by the first-mover advantage and leverage of substantial non-equity capital in the early stage right after the seed and start up financing, and the curve at early stage (Figure 1) become shallower and shorter to reach IPO before it could stretch up its profit curve up in the expansion stage.

4.0 CONCLUDING REMARKS

Over the past thirty years, technology platform-based business models evolved significantly in biopharma. Our observations based on four paradigm platform companies in different times suggests that the friendly, development environment of Millennium, as a pioneering “technology-insight” genomics platform company (rather than a therapeutic based platform) had experienced in 1990s, became rare. However, if you decide to build up a therapeutic platform company with aspirations to make sustainable achievement with remarkable valuations, the experience from the present paradigm companies like Alnylam, Moderna, and Kymera are insightful. Actually, the process of early stage strategic value creation from the four companies

described above indeed shared a lot more similarities and could shed some light on the future stars of innovative and transformative technology platform driven biotech.

1. The enabling technology platform model is still viable and timeline to an IPO is visibly shortened.
2. To make a paradigm success, the technology platform must be groundbreaking, ideally therapeutic nature, with broad range of application to create multiple product opportunities, in order to ensure the sustainable growth.
3. Platforms must be highly leverageable in order to raise non-dilutive, high-margin capital. Equity and partnerships need be carefully balanced. The quality and quantity of non-dilutive capital deals and partnerships with big brothers/partners in very early stage is a great indicator of valuation.
4. Relentlessly consolidate your platform, and build your own pipeline to keep sustainable competitive advantages.
5. Nowadays, biotech founders and entrepreneur need to work even more intimately with little brothers (early stage VC) in the start-up stage given the heavy funding needed in this period with timely and meaningful deliverables. Note they are very dilution averse and would like

to participate in all private financings until an inflection point.

6. Think about the context and timing when building up your platform company (political, capital market, science maturity). First mover obtains big advantages, so don't wait until science is fully ready, and we believe you will find a chance to adapt, pivot, and transform your company later. Perseverance is important!

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