NICHE STRATEGIES IN THE HEALTHCARE INDUSTRY

By

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Submitted to MIT Sloan School of Management on May 12, 2017 in Partial Fulfillment of the Requirements for the Degree of Master of Business Administration.

ABSTRACT

This paper examines niche strategies in the healthcare industry. I begin by discussing productivity trends in large firms. In order to understand trend shifts in productivity from a focus on output to a focus on input, I examine the competitive strategy frameworks of Duncan Simester of MIT, and Michael Porter of Harvard, and then apply these frameworks to the healthcare industry. That foundation allows me to develop the framework for a niche strategy.

There are two input reduction strategies, and I discuss each one based on the niche strategy framework. I also examine the role of healthcare start-ups and compare them with start-ups in other industries. Finally, I compare the growth strategies of incumbent large firms and start-ups in the healthcare industry.

Thesis Supervisor: Duncan Simester Title: NTU Professor of Marketing

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I dedicate this thesis to my wife and daughter.

Takahiro Hagisako Cambridge, Massachusetts May, 2017

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INTRODUCTION

The healthcare industry is facing a new wave of technology, similar to what is happening in other industries. All must adapt to this rapidly changing world by applying new strategies that enable them to succeed in this environment. Most pharmaceutical companies face the prospect (sooner or later) of losing their once-exclusive patents on earlier blockbusters, along with the continuing need to create new products, and identify and build new sources of future business. Having many healthy pipelines is a critical success factor for large pharmaceutical companies.

In this thesis, I analyze the approaches taken by large incumbent healthcare firms and start-ups vis-à-vis productivity and the strategies they are pursuing. I also contrast the competitive strategies of both types of firms in this environment.

PRODUCTIVITY

Organizations seek ways to increase their productivity in order to pursue effective operations and greater profitability. In general, productivity is defined as follows:

Figure 1. Productivity Equation

Typically, input is the amount of resources needed to produce products or provide services. Output is the amount of products, services, and revenues, etc., produced as a result of consuming the available resources. Productivity is currently measured in these ways: "revenue/cost", "revenue/number of sales reps", and "revenue/ number of employees." However, that is changing.

2.1 The Productivity Trend

The productivity trend in pharmaceutical companies is changing, especially among large firms that have always focused on increasing their output. Their primary purpose was to broaden the portfolio or expand coverage into new therapeutic areas by adding to the

drug pipeline in various ways, such as licensing from biotech companies and acquiring biotech start-ups. However, as recent and future trends are beginning to show, the large firms are shifting to a focus on managing inputs in order to reduce the resources consumed in the development and delivery of drugs. More specifically, firms want to reduce their drug development cost.

Research and development spending has been stagnant globally for the past several years, with the compound annual growth rate of global pharmaceutical R&D at 1.7% between 2008 and 2015 (Evaluate Pharma, 2016a).

COMPETITIVE STRATEGY

In order to explain the change in productivity trends from the business strategy point of view, I will begin by reviewing healthcare firms' competitive strategies in general. I aim to answer this question: What is the implication of this shift to productivity focus in the pharmaceutical industry?

Michael Porter defines three types of strategies, as shown in Figure 2.

Uniqueness perceived by customer Low cost position Industry wide Differentiation Cost Leadership Particular segment only

Figure 2. Porter's Three Generic Strategies

Source: Porter, 1980, Competitive Strategy (p. 39)

The *Strategic Advantage* dimension has two types of strategies: "uniqueness perceived by customer" and "low cost position."

The *Strategic Target* dimension has two approaches: "industry-wide" or "particular segment only."

Within this matrix, Porter defines three strategies: Differentiation, Cost Leadership, and Focus. Generally, large firms pursue the Cost Leadership strategy by optimizing their global operations, or they pursue Differentiation to build strength in certain therapeutic areas in the mass market. The Focus strategy targets a particular segment only, based on a uniqueness that has been identified by customers or because it is the low-cost approach. Pharmaceutical companies compete with each other by adopting one of these three strategies. This is a typical approach in other industries as well.

The pharmaceutical industry has become more segmented based on individual diseases that require specific knowledge and understanding of the disease occurrence and development. As the pathology advances, the mechanism of each disease is revealed, and the pathology is subdivided into smaller groups. There are also much clearer boundaries compared to other industries because of this scientific categorization and patent protections. Relevant consumers are defined by disease and are segmented systematically. As a result of this environment, we can say those firms generally pursue a Focus strategy.

Digging further into the Focus strategy, we can understand the key strategy and define a strategy that answers the question posed at the beginning of this section. If a firm targets small market segments and enjoys a monopoly market without competition, that strategy is called a niche strategy. A niche strategy is categorized within the Focus strategy.

THE ROLE OF NICHE STRATEGY

As I sought answers to the shift of productivity focus in large firms, this trend could be explained by the niche strategy. Indeed, the shift to input reduction is forcing large pharmaceutical companies to implement a niche strategy. As discussed in Section 3, pharmaceutical companies generally take the Focus strategy. The niche strategy is the ultimate strategy within the Focus strategy in terms of the size of the target segment and the competition. A niche strategy is adopted for a specific narrow target, and for a less competitive environment compared to a mass strategy. In a niche strategy, the consumption of resources is less than with a mass strategy. This is the reason why input reduction results in the niche strategy approach.

Duncan Simester defines the criteria for a niche strategy as follows:

- No large growth
- Barrier to entry
- Focus on profit

Typically, in the niche environment there is no competitor, certainly not at the beginning of entry into the market. A company may enter a certain market as a first entry, but once profitability decreases or competition becomes severe, the firm finds a new niche market and gain the benefits of being a first mover. This continuous movement into new

markets is the one of the key features of the niche strategy. A more detailed explanation is provided below.

4.1 Criteria for a Niche Strategy

- No Large Growth in terms of market size. This is the key feature of this strategy. Since the
 market is small, typically other firms are not interested in the market, sometimes not even
 noticing the existence of the market. The trade-off of such a niche strategy is smaller market
 size.
- Barrier to Entry in terms of the cost of preparation for entry. Since the niche market often has specific needs, in order to adjust requirements to target them, unconventional investment may be required if competitors want to enter the market.
- Focus on Profit in terms of selling the product or service. Since the market size is not large, if the firm does not focus on profit margin (profitability), what remains on hand could be very small. The firm would be better to pursue a high profit margin.

THE INPUT REDUCTION STRATEGY AS A NICHE STRATEGY

There are two types of input reduction strategies: Direct and Indirect:

Direct: the firm tries to reduce inputs in order to increase productivity.

Indirect: no direct reduction of productivity from the firm's perspective, but the strategy results in increased productivity from the perspective of other stakeholders such as patients, doctors, and payers (see Figure 3). This type of input reduction strategy is illustrated by using companion diagnostics that seek to avoid unnecessary drug use.

Type of input reduction	Description	Example		
Direct	Reducing input straightforwardly	Orphan Drugs		
Indirect	Reducing the input in an oblique way with positive externality	Companion Diagnostics		

Figure 3. Types of Productivity Input Reduction

Source: Thesis author

5.1 Direct Input Reduction Strategy: Increase Productivity by Reducing the Cost of Drug Development

The best example of the direct strategy is an orphan drug. According to the Orphan Drug Act of 1983 (ODA), an orphan drug is defined as one intended to treat a disease that affects fewer than 200,000 individuals in the USA (U.S. Food and Drug Administration, n.d.). At least 25 million Americans are affected with one of some 7,000 recognized orphan diseases (RDCRN, 2010). Given such small market conditions, pharmaceutical companies typically do not go into such a market proactively. However, the recent focus on the direct input strategy is forcing companies to apply a niche strategy. As a result, the number of orphan drugs in the market has increased in the past several years (see Figure 4).

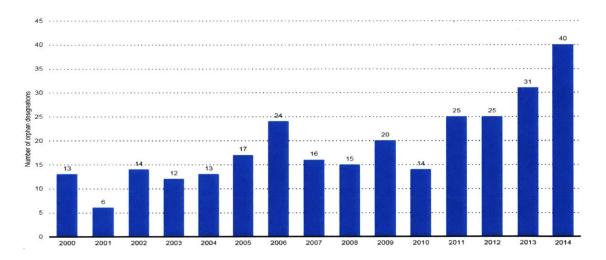


Figure 4. Number of FDA-Approved Orphan Drug Designations in the U.S., 2000-2014

Source: Statista (Evaluate), 2017

Even though the market size is small, if a firm carefully plans an orphan drug development and market entry, several benefits can be realized. It also builds a mutually beneficial environment for the pharmaceutical firms and patients who are suffering from these rare diseases.

Typically, the cost of orphan drug development is much lower than it is for common drugs, so it makes economic and financial sense for pharmaceutical firms (Evaluate Pharma, 2016b). The cost of a clinical trial is typically lower since the number of patients required for the test is fewer than is required for testing of common drugs. Additionally, the U.S. government provides tax benefits to the firms, and gives the firm seven years of exclusivity in the market (Hughes & Poletti-Hughes, 2016) This is an obvious example of productivity increase by input reduction.

In terms of entry into the market, a firm initially enters a single-indication drug only for a specific disease. It first creates the drug that targets a single disease (the primary approval), and then continues to add new indications and move into new markets (the secondary approvals) (see Figure 5). Consistent with the definition of a niche strategy, this is precisely the niche strategy approach.

This standardized solution facilitates a growth strategy when a firm continually enters new markets (new niches). In this orphan drug example, most of the core drug function was verified by the first indication approval. For the second indication, obtaining approvals is generally easier and faster because firms can use their accumulated information and knowledge from the first indication. The documentation required for the approval is also less.

Orphan Approvals By Year

First-time orphan approvals have more than doubled over the past decade, with a record 37 of them in 2015. These approvals include new molecular entities, other new drugs and repurposed drugs approved as orphans for the first time. But companies continue to get secondary orphan approvals to treat additional diseases — or sometimes just slices of those diseases. In fact, in 2006, there were more second-time orphan approvals than first-time orphan approvals.

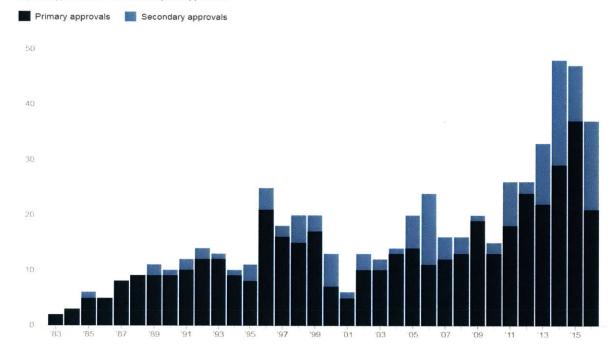


Figure 5. Primary and Secondary Approvals of Orphan Drugs, by year (NPR, 2017)

Source: FDA's Orphan Drug Database, Kaiser Health News

Interestingly, it is possible for the opposite approach to occur as well. Some drugs are first approved as common drugs for the mass market. Later they may be designated as orphan drugs if they target a specific disease as a result of additional research and development. Some of the top drugs in the country in 2015 were first approved for the mass market, and later won approval for a rare disease (see Figure 6).

Seven of the 10 best-selling drugs in the country in 2015 were orphan drugs. Some of these drugs are not "true" orphans, critics say, because they were first approved for the mass market and later won approval for a rare disease.

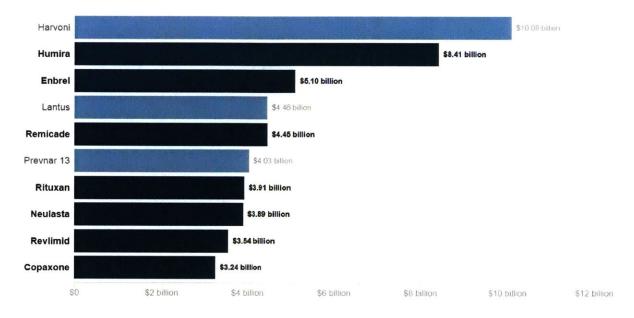


Figure 6. Top 10 Best-Selling Drugs (NPR, 2017)

Source: FDA's Orphan Drug Database, Kaiser Health News

5.2 Indirect Input Reduction Strategies: Increase Productivity by Avoiding Unnecessary Drug Use

A good example of an indirect input reduction strategy is companion diagnostics. A companion diagnostic is a medical tool, such as an *in vitro* device, that provides essential information for the safe and effective use of a relevant drug or biological product. An explanation on the FDA website states that the test helps a healthcare professional determine whether a particular product's therapeutic benefit to patients will outweigh any potentially serious side effects or risks (U.S. FDA, 2017). Companion diagnostics can:

Identify patients who are most likely to benefit from a particular therapeutic product

- Identify patients likely to be at increased risk for serious side effects as a result of treatment with a particular therapeutic product
- Monitor response to treatment using a particular therapeutic product for the purpose of adjusting treatment to achieve improved safety or effectiveness.

Utilizing a diagnostic before actually using a drug allows checking the patient in advance, thus avoiding unnecessary drug use. The companion diagnostic is responsible for assessing how effectively the drug will work in a specific person, and can be used before the medicine is actually taken. As a result, the patient avoids taking a drug unnecessarily, and they believe they are receiving more accurate treatment. This strategy creates an entry barrier for competitors while targeting specific patients. Once a layer of patients is identified within a disease, the market is secured for the drug. The combination of diagnostics and targeted drugs create a unique segment. This market cannot easily be threatened by competitors. Typically, the diagnostic tools are also protected by patents. All of these factors are part of the niche strategy approach. This indirect approach has been deployed widely, particularly in oncology (see Figure 7).

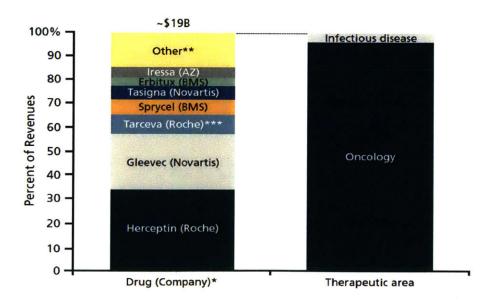


Figure 7. Worldwide Companion Drug Revenue, 2013

Source: Vadas & Baranick, 2015

In addition to the traditional biomarker approach as a recent trend of companion diagnostics, novel technologies have come under the spotlight. Large firms are partnering with start-ups to effectively develop companion diagnostics tools (see Figure 8).

PM trends		Biopharma company(ies)	Partner	Description		
Adoption of PM outside oncology		Takeda	Quest Diagnostics	Genotyping test for APOE status and TOMM40 polymorphism for Alzheimer's		
		Merck	Luminex	Immunoassay for Amyloid 42 and tau in mild cognitive impairment		
	More efficient clinical trial enrollment	Amgen, Genentech, Pfizer, AZ	Foundation Medicine	Lung Cancer Master Protocol collaboration		
	Improved sample access	AstraZeneca	Qiagen			
Increased competition		Bayer		Liquid biopsy approaches in a sample constrained environment		
in oncology		Merck KGaA	Sysmex			
	Improved CDx predictive power	Amgen	Illumina	NGS panel test for KRAS and NRAS		
		GSK	BioMerieux	PCR panel test for V600E and V600K		
Movement beyond oncology therapy selection to monitoring		Arno Therapeutics		Enables disease/therapy monitoring		
		Novartis	Veridex			
Exploration of nuanced cancer biology		Eli Lilly	Qiagen	Detection of both DNA and RNA biomarkers for oncology		
		BMS	IncellDx	Multimodal technology for cell-based protein and gene expression analysis		

Figure 8. Examples of Novel Technology Partnerships

Source: Vadas & Baranick, 2015

Because of the nature of low-cost development and the unique regulation of orphan drugs, start-ups can contribute to the drug development process without investing a huge amount of money. This contrasts with mass market drugs, where start-ups are not as well positioned. I discuss the role of start-ups and incumbents in the next chapter.

THE ROLE OF START-UPS

Most start-ups focus on a novel functional innovation, then verify that a market exists using a proof of concept. Other industries have witnessed the disruptive impact of start-up activities. In the healthcare industry, I believe disruption by start-ups is less likely for two reasons:

- The healthcare industry is heavily regulated by the government. If the market is regulated, the advantages of a start-up are often diminished because they are unable to take advantage of their agility. In addition, enormous cost and effort are required in order to negotiate with the government, and it takes time to change regulations or deregulate key rules related to the core of the healthcare business model. Uber is a good example of this, although its regulations are much different from those of the pharmaceutical industry. If a regulation is directly related to human life, the level of regulation is much tighter, and the government is very cautious about making changes.
- 2) Ultimately, patients are served only by a specific person, typically a doctor. If that point of contact is limited, growth is inhibited because the resource is constrained, which often diminishes the effects of disrupters.

A lack of sufficient financial resources as well as segmented markets hinder the growth of a disrupter. In the healthcare industry, the percentage of R&D spending is very high compared to other industries (see Figure 9). Those factors contribute to promoting a

non-disruptive approach while enhancing the co-existence of large firms and start-ups. Large firms are often forced to standardize in order to maintain efficiency while continuing to grow. However, standardization can be a barrier to innovation in niche pharmaceutical markets, where specialization and customization are required. This provides an opportunity for small firms to play an important role. These small firms provide the agility needed to specialize, which can complement the standardization and scale provided by large firms.

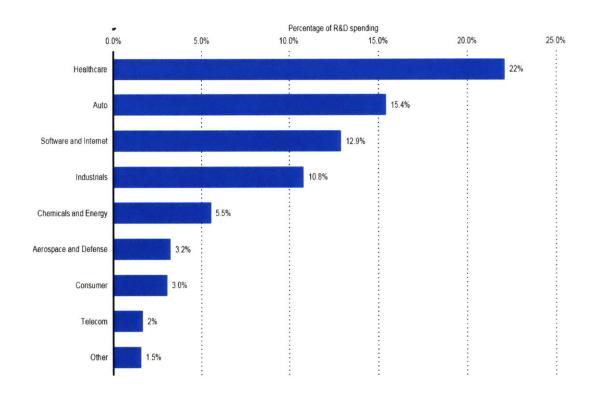


Figure 9. Percentage of Global R&D Spending in 2016, by industry

Source: Statista (Bloomberg; Booz & company), 2016

INCUMBENT FIRMS AND START-UPS: RESPONSES AND GROWTH STRATEGIES

As stated in Section 6, start-ups play a key role in developing new drugs and novel technologies. Large incumbent firms try to develop new drugs and technologies on their own, but their main growth strategy typically becomes acquisition of start-ups. To this end, large firms implement one of two strategies:

- Mergers and Acquisitions (M&A): For start-ups, the growth strategy is to be acquired by the
 large incumbent firms. Thus, in the healthcare industry, M&A is a key growth strategy for both
 players, which developed into a win-win environment that has been implemented with
 regularity over recent decades.
- Customizing at Scale: a strategy sometimes taken by large firms.

I discuss both strategies below.

7.1 Strategies of Large Incumbent Firms

7.1.1 Mergers & Acquisitions

Among large pharmaceutical firms, mergers and acquisitions of start-ups is the traditional approach taken. Even if a merger between companies is not officially achieved, the firms may be willing to partner in order to use the start-up as a source of new technologies and new drugs.

However, the objective of an acquisition is likely to be different from what typically occurred in the past. With the trend toward reducing inputs, the purpose of an acquisition these days is often to undertake R&D more economically rather than to broaden the large firm's technology portfolio (see Figure 10). Instead, such acquisitions enable the large firms to align more closely to their growth strategies.

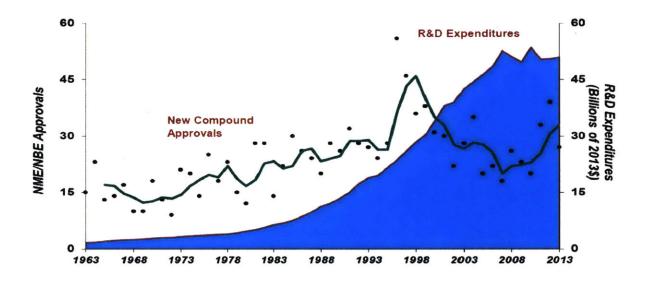


Figure 10. New Drug and Biologics Approvals, and R&D Spending

Notes:

R&D expenditures are adjusted for inflation.

Curve is a 3-year moving average for NME/NBEs

NME = New Molecular Entities

NBE = New Biological Entities

Source: Tufts Center for the Study of Drug Development, 2014

A study conducted by the Tufts Center for the Study of Drug Development (2014) found that in recent years, R&D is not scalable, which is another reason why large firms

continue to pursue the M&A strategy. Especially in the past ten years, the amount of R&D spending does not correlate with new compound approvals. Increasing R&D expenses is becoming unsustainable within large firms. The blockbuster model focusing on lifestyle-related diseases is in decline and is being replaced by a personalized and niche-market-oriented drug development model (Okuvama & Osada, 2014).

Looking at recent and future trends, there are several key questions that firms should consider before implementing a strategy. Borrowing from Simester's framework, some questions might be:

- When does M&A work as a growth strategy for large firms?
- Will the technology or drug held by a start-up really meet the patient's need?
- Will the acquired technology or drug become a strategic resource for large firms?
- If yes, will it meet these criteria for strategic resources:
 - o ownership & control
 - o differentiation
 - o sustainable
 - contribute to satisfying customers
- Will the acquisition be the best choice for delivering value to the patients?
 These questions should be answered carefully as firms consider their acquisition and growth strategy and prior to making a decision.

Typically, patients acknowledge the value of a new drug by using it, especially if they experience at least some relief or perhaps even a cure. However, for large firms, capturing value is more complicated: if they opt to pursue M&As as a growth strategy, often there is no end until one company eventually dominates the market. But in the pharmaceutical industry, this scenario is unlikely because it is hard to imagine the perfect drug that will cure

a disease completely, especially when talking about oncology as the largest market. In that sense, firms have to assess the questions posed above, especially as they look to capture value.

7.1.2. Customizing at Scale

Another response taken by some larger firms occurs when mass market players respond by integrating and customizing at scale. According to Ariker, et al. (2015), customizing at scale requires the integration of three things: data discovery, automated decision making, and content distribution. This type of response can be illustrated using my earlier example of a large firm applying the framework to companion diagnostics. The diagnostic device can discover and specify people who should be treated, and that decision will be automatic when the diagnostic device is used. Large firms typically have a huge network for distributing this device, thus enabling the firms to implement the customization in an integrated manner.

Additionally, thanks to advanced technologies, large firms can take advantage of predictive analytics, machine learnings, and artificial intelligence to customize and personalize at scale by using the enormous amount of data available in the market. Such an example is the patient's support practice at Biogen for people with multiple sclerosis. Biogen provides specially prepared information for people who are living with relapsing MS, as well as from professional experts in areas such as financial planning, cooking, and exercise (Biogen, 2017). The firms continually integrate the information and data that comes to them, and provide it to patients as a personalized service. At this stage, I am

assuming that the Biogen service is not yet equipped with automated decision making by AI, but this is a good example of a large firm's response to customizing at scale.

7.2 Strategies of Start-ups

For start-ups, it is crucial to highlight key factors that make them excellent candidates for M&A, for example:

- Their robust technology makes the start-up a strong possibility for acquisition
 (even though it may be in a very early stage)
- 2) Evidence that shows the remaining steps needed to complete clinical trials and the support needed from a large firm, in order to attract the firm's investment
- 3) Evidence of the robust nature of the drug or technology as an intellectual property. Protection by patent is mandatory in this approach.

Today, venture capitalists and other third parties have the capability to assess technologies and drug candidates, which enables them to take a systematic approach to measuring the risk and return on their investment. For example, they may know the appropriate approach to solving a problem (i.e., curing a disease). Some drugs block the transmission of a certain protein, others target a specific gene to intervene in the generation of the protein. In terms of orphan drugs, there is generally no correlation among diseases biologically, and it is easy to build a portfolio without measuring the overall risk. Large pharmaceutical and medical device firms use these third-party investors as an indicator of preliminary selection.

Since having an excellent technology or drug is critical, start-ups must have a strategic communication plan in order to achieve their goal of acquisition by a large firm. Otherwise, most start-ups will not remain in the light forever. This is one reason why storytelling and strategic messaging are popular among start-ups in their early stages of growth.

As Figure 11 shows, early-stage acquisition is becoming more popular. I believe this is because of advancements in the technology, whereby people now understand more clearly the mechanism of a disease, which in turn enables an earlier decision to acquire. As the certainty increases, so too will the price, and large firms want to secure a new technology at an earlier stage if it means a more reasonable price.

Acquirers Flock to Early-Stage Biopharma Companies

VC-backed Biopharma Big Exit M&A by Stage 2012-2016

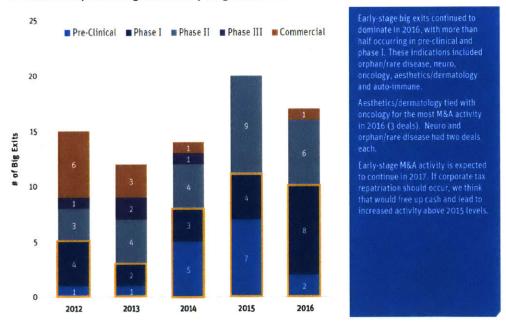


Figure 11. Exit Timing of Biopharma Companies

Source: Norris & Peralta, 2017

This tendency is especially apparent with the acquisition of orphan drugs, often resulting in remarkably quick exits (see Figure 12)—sometimes only 1.5 years from the time of raising Series A equity (Norris & Peralta, 2017). Thus, as start-ups pursue a more niche strategy, they can demonstrate more value to large firms or investors since there will be clear differentiation and a specific market.

Oncology, Neuro Lead Biopharma Big Exits; Orphan/Rare Disease Gains Early-Exit Traction

VC-backed Biopharma Big Exit M&A by Indication 2012-2016

	Number of Exits	Median Years to Exit	Pre-Clinical	Phase I	Phase II	Phase III	Commercial
Oncology	18	4.3	8	4	4	0	2
Neuro	13	4.2	4	1	5	1	2
Respiratory	7	4.9	0	1	4	1	1
Aesthetics/Derm	6	6.1	0	2	2	0	2
Cardiovascular	6	5.7	1	2	1	0	2
Auto-Immune	5	3.7	2	2	1	0	0
Anti-Infective	5	5.6	1	3	1	0	0
Orphan/Rare Disease	4	1.4	1	1	2	0	0
Ophthalmology	3	4.1	0	0	2	1	0

Oncology saw the highest number of big exits since 2012, and 12 of 18 were early stage (pre-clinical or phase I).

Orphan/rare disease has attracted significant venture investment in recent years, and now we are seeing remarkably quick exits: 1.5 years from Series A equity raise. Six of 9 indications (highlighted above) have a median time to exit of 5 years or less.

Figure 12. Number of Years to Exit of Biopharma Companies

Source: Norris & Peralta, 2017

One common obstacle to the acquisition of start-ups by large firms is known as the "Lemons Problem" (Akerlof, 1970), which refers to issues that arise when the seller has asymmetric information about the value of the asset (INVESTOPEDIA, 2017). The seller's

willingness to sell often becomes a signal that value is low, which can discourage potential purchasers.

However, the pharmaceutical industry is an exception, as the Lemons Problem does not prevent early-stage acquisition of drugs. One explanation for this is that there is no asymmetric information – the buyer has the same information as the seller. The staged drug development process and contract terms facilitate this. This does not mean that all of the information is complete. There is considerable uncertainty about the effectiveness of new drugs, which is only resolved by conducting clinical trials.

CONCLUSION

As I have shown in this thesis, large firms are shifting their strategy to a focus on input reduction in term of productivity. This trend can be explained by two types of approaches: direct and indirect. Currently, there is little in the literature that discusses and defines a niche strategy, even though the word "niche" is widely used today. Despite this, my research found that the shift by large incumbent firms to a focus on inputs is forcing a niche strategy, and I found obvious connections between them. When considering small markets, it is easy to speculate that a small player might do better compared to large players, which is why start-ups are playing a key role in the segmented market of the pharmaceutical industry. I found that start-ups are exploring niche strategies wisely and cleverly.

In the healthcare industry, the ecosystem is being developed in a collaborative way, and there is little competition between large firms and start-ups. They cooperate with each other and mutually complement one another while they look in similar directions for patients.

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