Impact of genomics on biopharmaceutical industry: rare diseases as disruptive innovation

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Abstract

Purpose – Using a dynamic capabilities lens, this paper aims to study the impact of genomics generally and gene therapy specifically on the rare disease sector of the biopharmaceutical industry.

Design/methodology/approach – In this study, 24 genomics-based, rare disease-focused biopharma companies were studied and several variables were tested with respect to enterprise value growth. The companies were analyzed as a group of rare disease firms, as well as by size.

Findings – The authors found that number of employees, revenues, number of pipeline and marketed products and retained earnings are strongly correlated (in that order) with enterprise value in rare disease focused biopharma companies. These correlations seem to be weaker as a company's market capitalization size decreases, indicating that there tends to be increasing returns to scale.

Research limitations/implications – This study found that increasing rates of cumulative returns to enterprise value growth depends on accumulating knowledge-based employees and expanding product portfolios of disruptive genomics-based technologies for treating rare diseases. Aggregating skilled and innovative employees (especially in bigger companies) can be seen as a cumulative bolstering factor in leveraging dynamic capabilities which can be recognized, understood and transformed into commercial success (i.e. increasing returns in enterprise value). In other words, technology managers' job is to manage not only the financial aspects of the technology but also human resources, asset configuration and strategic alliances efficiently toward faster and better innovation. Strong dynamic capabilities can be formed with the accumulation of experience, articulation and codification of knowledge and an adaptive ability to change the way they solve problems as their environment transforms.

Originality/value – This is the first study to demonstrate and measure a relationship between dynamic capabilities and enterprise value in genomics-based rare disease firms. Further, this study highlights the importance of building the capability and capacity to absorb expertise and accumulate knowledge for new product innovations and sustainable competitive advantage in industries characterized by disruptive innovation.

Keywords Dynamic capabilities, Genomics, Rare diseases

Paper type Research paper

1. Introduction

Multinational biopharmaceutical firms grapple with intense financial pressures because of an increasingly cost-constrained and highly regulated health-care environment, finite patent expiration on blockbuster drugs, generic competition, decreases in effective market exclusivity from new innovations and a proliferation of smaller markets because of the escalating genetic segmentation of patient populations. Specifically, because of dramatic cost reductions in DNA sequencing following the development of "next-generation" platforms, molecular diagnostics are increasingly being considered to be cost-effective enough to be used as a standard medical test, both prospectively for risk assessment and confirmation of diseases – and increasingly, as therapeutics for rare diseases. In the midst of

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these developments, pharmaceutical companies are obliged to reevaluate their drug development strategies and business models (Niosi and McKelvey, 2018; Jeon *et al.*, 2016; Downs and Velamuri, 2016; Shaygan, 2018).

In contrast to the prevailing large, multinational pharmaceutical model (e.g. Merck, Pfizer, Roche and Glaxo), where there was a reluctance to invest in rare diseases because of small addressable patient populations and limited markets, biopharmaceutical companies are gaining increased investment interest in rare disease treatment. Currently, there are 30 million Americans suffering from approximately 7,000 rare diseases (only 5 per cent of these conditions have approved treatments) (Piccart-Gebhart, 2013; Medicines in Development, 2016). Among many technological advancements, one that has undoubtedly had a great influence on this economic shift is the DNA (deoxyribonucleic acid) sequencing and mapping of the human genome. Driven by Sanger-based advances, the cost of sequencing a human-sized genome has fallen dramatically from $100m to $1,000 in the past 25 years (Mardis, 2008; Wetterstrand, 2016). Some of the other reasons behind the increasing interest in rare diseases from pharma companies are the significantly less product development time needed in terms of patient testing, increased government financial incentives, pediatric review voucher and higher approval rates from US Food and Drug Administration (FDA, 2015).

As such, the genomics revolution is poised to significantly disrupt traditional multinational pharmaceutical industry structure, which relies on large, blockbusters of chronic medications aimed at large patient populations. Building on precursor technologies such as enzyme replacement therapies, which require continuous treatment, these disruptive innovations such as gene therapy, which delivers single treatment cures, will significantly shift the biopharmaceutical industry structure and business models to stay relevant in such high-velocity markets. In existing literature, there is a gap in demonstrating and measuring the relationship between dynamic capabilities and enterprise value in technology-based companies generally and genomics-based rare disease firms specifically. Using the lens of dynamic capabilities, we explore the effects of different financial, organizational and product-related assets on the enterprise value of rare disease-focused biopharmaceutical companies. This study will also look into the importance of different components of business model development in specific biopharma companies and their role in their success. Next, we review the background of the biopharma industry and the influence of genomics in rare diseases generally and gene therapies specifically (delivery of single treatment cure using corrective genes for fatal rare diseases) (Figure 1).

2. Biopharmaceutical industry

The biopharmaceutical industry is a combination of traditional multinational drug manufacturers, biotechnology companies and distribution companies mainly concentrated on medicinal and veterinary chemical and biological combinations. A pharmaceutical company can be characterized as a firm that performs commercial research and development, marketing and distribution of drugs (McGuire *et al.*, 2007). Biotechnology refers to techniques for changing microorganisms, and a biotechnology firm is a company that develops products based on influencing living cells (plants or animals) using biological expertise and knowledge (Shan *et al.*, 1994). In highly dynamic industries with intense global competition and entrepreneurial high-tech organizations such as pharmaceuticals and biotechnology, new product development is one of the most significant factors of success (Deeds *et al.*, 2000). Thus, drug development companies have been shifting their strategies

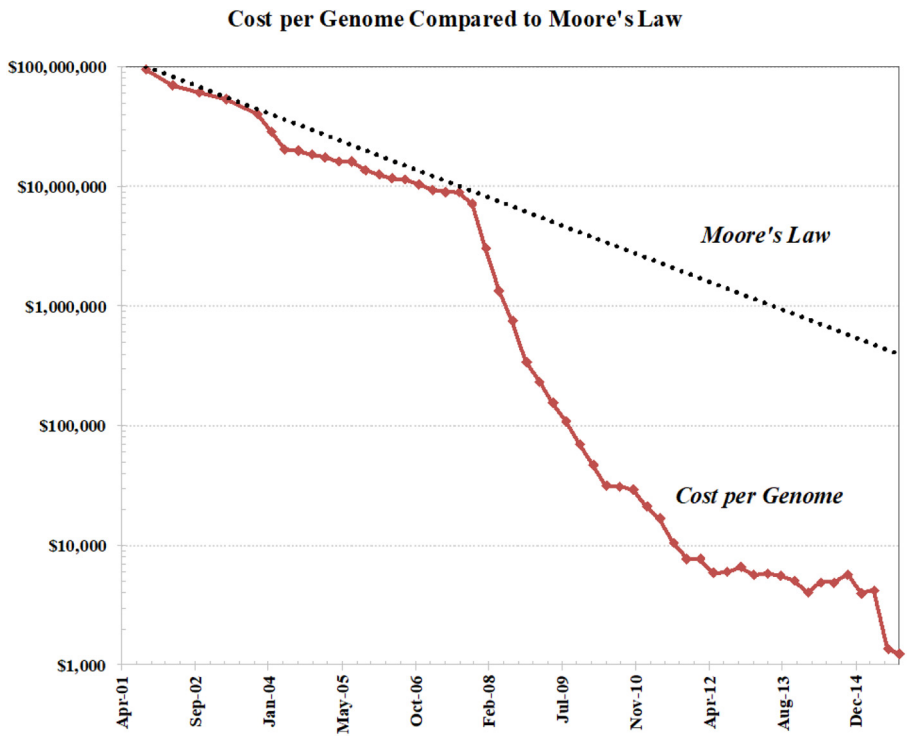

Figure 1. Cost per genome evolution compared to hypothetical data reflecting Wetterstrand (2016)

from manipulating natural compounds to use of new biologic understanding and tools to research and develop new drugs (Casper and Matraves, 2003; Ahn *et al.*, 2010).

New genomic insights and tools such as gene therapy, regenerative medicine and molecular diagnostics are driving a fundamental industry shift from active disease confirmation to treatment decision-making, avoidance and wellness (Biotechnology Industry Organization, 2006). As one of the largest employers of scientists and one of the highest levels of R&D among industries (increasing R&D expenditure from $2.0bn in 1980 to $51.4bn in 2014 in USA), the pharmaceuticals industry addresses large global markets (Ahn *et al.*, 2010; PhRMA, 2015). Of note, the USA comprises 86 per cent of global biotech financing (Ernst and Young, 2016). Some of the other characteristics of this industry are long drug development times (10-12 years), low levels of drug transformation from clinical trials to approved drugs (less than 12 per cent), high drug development costs (from $179m in 1970s to $2.6bn in 2000s-early 2010s) and high R&D expenditure as sales fractions (23.4 and 17.9 per cent for domestic and total sales, respectively) (PhRMA, 2015; Dimasi, 2014). Ernst and Young (2016) noted that 78 biotech companies went public and raised $5.2bn in their initial public offerings (IPOs), of which 45 were from the USA. Multinational pharma and biotech companies are emphasizing the importance of strategic alliances in building their pipelines (Ahn *et al.*, 2009, 2010).

One of the more disruptive sub-sectors of the biopharma industries is genomics which affects different sectors of the industry such as companies that focus on single treatment

cures for rare diseases. Thus, many companies are significantly increasing R&D investment in genomics to tap the market for rare diseases and leverage the new opportunities to treat heretofore unmet medical needs.

2.1 Genomics and rare diseases

Genomics, which is defined as the scientific discipline of sequencing, mapping and characterization of human genes, has significantly influenced drug discovery and development in the pharmaceutical industry (Emilen *et al.*, 2000; Venter *et al.*, 2001). Molecular genetics has fundamentally changed drug development in terms of assessing risk, early detection and targeted therapies for devastating unmet medical needs (Khoury *et al.*, 2011).

In the past two decades, the cost of sequencing a human-sized genome has fallen dramatically from $100m to $1,000 and sequencing industry leader Illumina is aiming for a $100 genome. The sudden change of speed and per genome cost reduction since 2008 reflects the transition from Sanger-based sequencing to next-generation genome sequencing technologies (Mardis, 2008). The emergence of next-generation sequencing technologies in the marketplace has enabled the production of an enormous volume of data inexpensively (up to 1 billion short reads per instrument run) (Metzker, 2010). The information that genomics provides can bolster our understanding of disease biology, personalized therapies and health-care decision-making (Green and Guyer, 2011; Calzone *et al.*, 2013).

As such, the treatment of rare disease has been one of the biggest and most disruptive windows of opportunity opened by the progress in genomics. Rare diseases provide researchers with smaller populations of patients, and an opportunity to cost-effectively develop drugs spanning across highly non-homogeneous spectrums of diseases within a specific genetic disorder (Pariser, 2014). A rare disease is defined by the Rare Disease Act of 2002 as "any disease or condition that affects fewer than 200,000 people in the USA" (107th US Congress, 2002). Genomics is helping researchers to better understand the nature, severity, rate of progression and clinical presentation of these diseases, many of which affect pediatric populations. More practically for smaller biopharma companies, the increased interest in rare diseases is also piqued by smaller clinical trial populations, increased government financial incentives and higher approval rates from US Food and Drug Administration (FDA). FDA Commissioner Scott Gottlieb noted that:

> New guidance on the clinical evaluation of targeted therapies for rare disease subsets by the FDA. . .will address the issue of targeted drugs, and how we simplify the development of drugs targeted to rare disorders that are driven by genetic variations, and where diseases will all have a similar genetic fingerprint (Biocentury, 2017).

For example, Avexis, Inc. is developing AVXS-101 (gene therapy) for the treatment of Spinal Muscular Atrophy, which is uniformly fatal by two years of age (Campos Araujo *et al.*, 2009; Mendell *et al.*, 2017). This disease is caused by a single genetic defect, and Avexis has the goal of mitigating or treating this disorder using a single treatment gene therapy. Initial results presented in 2017 demonstrated that 15 of 15 (100 per cent) patients were event-free at 13.6 months (versus an expected event-free survival rate based on the natural history of the disease of 25 per cent). Many companies such as Avexis, Biomarin, Bluebird, Abeona, Dimension and Spark are targeting different debilitating, genetically based rare diseases.

Many of these biotech firms enter strategic alliances with larger firms to leverage resources and attain validation (Ahn *et al.*, 2010; Eisenberg *et al.*, 1998). Some of the examples are Bluebird bio's partnership with Celgene or Spark Therapeutics partnership with Pfizer in the development of SPK-9001 drug for the treatment of Hemophilia B (Draper *et al.*, 2015). Another important aspect of these rare disease-focused biotech companies is that they are co-located in biotech clusters such as New England and California which account for 17 of the 24 studied companies. Biotech clusters enhance access to academic research centers, qualified employees, experienced vendors and suppliers, informed life science venture investors and shared resource arrangements (DeCarolis and Deeds, 1999; Ahn *et al.*, 2009; Ahn *et al.*, 2010; Al-Khateeb *et al.*, 2016).

Ultimately, industry sectors rise by creating, building and capturing value. While the biotech sector has dramatically outperformed the S&P 500 index (which represents the US stock market index based on the market capitalizations of 500 large companies having common stock listed on the NYSE or NASDAQ), the Rare Disease sub-sector of the biotech market has experienced extraordinary growth (Figure 2).

In sum, biopharma companies need to acquire dynamic capabilities to recognize, understand, transform and exploit their tangible and intangible assets (tacit knowledge, R&D know-how, new product development, partnerships and acquisitions, and skilled workforce attraction) to accelerate innovation (Collis, 1994; Zahra and George, 2002). Markets such as biopharma are finely tuned to recognize and assess value, manage risks and reward companies who innovate in targeted therapies (Ahn and Meeks, 2008;

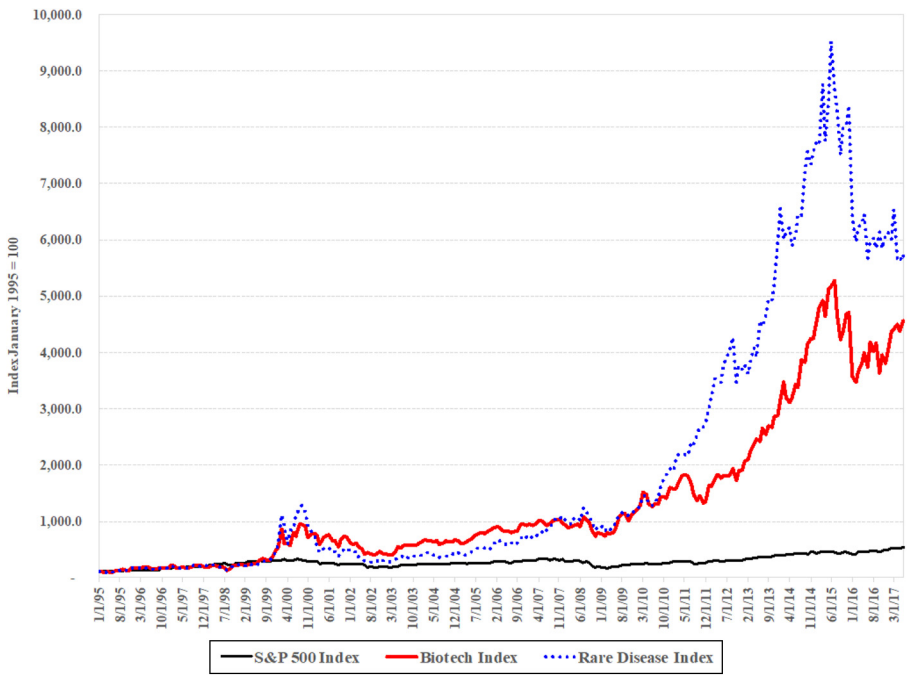

Figure 2.
Stock market performance: S&P 500 vs biotechnology v rare disease companies

Al-Khateeb *et al.*, 2016). Of note, this study considers all 24 publicly traded rare disease, gene therapy-focused companies in the USA at the time of the study.

3. Dynamic capabilities

In the technology-based world of new product development, faster information flow, easier access to global markets, managing intangible assets and the way companies orchestrate them are keys to building unique value and competitive advantage (Teece, 1998). Teece *et al.* (1997) suggest that competitive advantage is built and protected not in product markets but in markets for know-how and other intangibles which they refer to as the dynamic capabilities.

There are multiple definitions of dynamic capabilities in the literature. Pisano (1994) defines them as organizational and strategic routines that allow managers to change, jettison, integrate and re-connect resources to create new value-generating blueprints (Grant, 1996). Dynamic capabilities are tools for generating, evolving and morphing of resources to attain sustainable competitive advantage (Teece *et al.*, 1997; Henderson and Cockburn, 1994). By merging these definitions, Eisenhardt and Sull (2001) define dynamic capabilities as the company's organizational and strategic actions to use, integrate, recombine, acquire and dispose of resources to equal or generate market change as a response to emergence, evolution, division and demise of markets (Eisenhardt and Jeffrey, 2000). Some of these actions can be alliances, acquisitions, new product development and strategic decision-making (Ahn *et al.*, 2013).

Moreover, Eisenhardt and Jeffrey (2000) posited several commonalities amongst dynamic capabilities across high-tech organizations. Although dynamic capabilities differ across various firms, technology-based firms possess some common traits such as being "equifinal" (reaching dynamic capabilities from different roads and being path dependent), "compatible" (effectiveness of some capabilities across different industries) and "dependent on market animation and learning methods" (Zollo and Winter, 1999; Eisenhardt and Jeffrey, 2000; Winter, 2003). In the context of the accelerating genomics-based pharmaceutical and biotech markets, dynamic capabilities are dependent on the generation of new knowledge for increasingly specific patient populations. Finally, firms with dynamic capabilities use unique types of adaptive knowledge creating activities as real-time information, prototyping, multi-criteria decision-making and experimenting in an iterative and cognitive way, which leads to unpredictable outcomes (Eisenhardt and Jeffrey, 2000).

Biopharmaceutical companies have to deal with fast-changing markets and rapid learning processes (York *et al.*, 2012). This environment can stress the importance of learning from experience as a way to generate dynamic capabilities (Gersick, 1994). Studies demonstrate that the learning mechanism, rather than detailed *a priori* plans, plays an important part of the evolution of dynamic capabilities for firms. Repeated practices (in activities such as acquisitions, integration and resource jettison) which lead to specific and tacit knowledge gain can be crucial for firms (Zollo and Singh, 1998; Argote, 1999; Brown and Eisendhardt, 1997). What is more important about learned knowledge is a company's ability to systemize, articulate, share and embed them into procedures and know-how which leads accelerated organizational learning (Argote, 1999; Eisenhardt and Jeffrey, 2000; Kale *et al.*, 2002; Zollo and Winter, 2002). Moreover, managers must acquire information from mistakes, failures and crises (real time and/or simulated scenarios) (Kim, 1998; Eisenhardt and Sull, 2001; Barreto, 2010).

Experience and speed can also bolster the creation of dynamic capabilities, as rapidly acquiring experience can strengthen managers' decision-making ability, bolster knowledge

and sharpen insights (Argote, 1999; Eisenhardt and Jeffrey, 2000;Teece *et al.*,2016). Another important factor that should be accounted for in fast-changing markets is the importance of experience in selecting and jettisoning products and businesses based on distinctive market changes (Gersick, 1994; Sastry, 1999). Finally, sequence appears to be important in generating dynamic capabilities (Brown and Eisendhardt, 1997; Eisenhardt and Jeffrey, 2000). By assuming that dynamic capabilities are modular and composed of smaller components (ingredients), the order of composition and implementation of smaller modules into a dynamic capability (recipe) is crucial for firms.

More recently, Pisano describes a firm's capability development as a problem of selecting between different identification strategies needed for its environment. That is, each firm has to choose to go deep or broad, general or market-specific in terms of dynamic capabilities (Pisano, 2017).

In sum, competitive advantage in high tech environments such as biopharmaceuticals is often episodic, fleeting and erratic. Hence, constantly acquiring, reshaping intangible assets and resources (sensing, seizing and transforming) to form and orchestrate dynamic capabilities is crucial to firms' success.

4. Hypotheses, data collection and methodology

Next, we consider the disruptive biopharma sub-sector of rare disease being driven by advances in genomics to consider elements of dynamic capabilities in building, creating and capturing value. We used the Biocentury database which tracks over 1,300 public and 4,000 private biotech companies worldwide from 1995-present. We identified 24 publicly traded rare disease-focused biotech companies, 18 of which focus exclusively on gene therapy during 1995-2017 (Biocentury, 2017). The rationale for choosing these companies is they represent all publicly traded, gene therapy-focused companies (i.e. public companies publish financial, as well as stock market performance data). In the USA, a rare disease is defined as one that affects fewer than 200,000 people. According to the Genetic and Rare Diseases Information Center (GARD) at the National Institutes of Health, there are over 7,000 rare diseases with less than five percent having an approved treatment. The studied companies are primarily concentrated in biotech clusters located in Massachusetts and California (Figure 3). The data were collected in the first week of May 2017.

Data were collected for each company in 11 categories (revenue, enterprise value, net income, retained earnings/total financing, cash, number of employees, CEO tenure, number of board of director members, year of foundation, year of IPO, clinical/commercial products and number of total products). The definition for each of these criteria is shown in Table II. The enterprise value (EV), which represents firm value generated with invested capital, has been defined as follows (Koller *et al.*, 2010):

$$\begin{aligned} \textit{Enterprise Value}\,(EV) \;=\; & \text{market value of common stock} \\ & + \text{market value of preferred equity} + \text{market value of debt} \\ & + \text{minority interest} - \text{cash and investments} \end{aligned}$$

Descriptive statistics for the collected 24 companies are shown in Table I.

The drug development process is lengthy and risky, with development times of 7.5 to 19 years (Dimasi *et al.*, 2003). To determine the status of each company in terms of new product development, data from their drug pipelines were collected for discovery, preclinical, Phase 1-3 and commercialization. The feasibility, iterative testing and safety-related information is

Figure 3.
Geographical locations of rare disease-based, gene therapy companies

	N	Range	Minimum	Maximum	Mean	SD
Enterprise value (million)	24	$27,816	−$46	$27,770	$2,751.68	$6,199.31
Revenue (million)	24	$3,011	$0	$3,011	$273.40	$681.68
Net income (million)	24	$1,029	−$630	$399	−$118.39	$175.98
Retained earnings (million)	24	$2,984	−$1,166	$1,818	−$277.44	$538.74
Number of employees	24	2,909	15	2924	400.50	712.92
CEO tenure	23	14.5	0.5	15	4.71	4.15
Number of board	24	6	5	11	8	1.47
Year founded	24	40	1974	2014	2002.04	10.96
IPO year	24	20	1996	2016	2010.08	7.13
Clinical and marketed	24	13	0	13	4.08	3.48
Total pipeline	24	25	1	26	8.70	5.47

Table I.
Descriptive statistics for the studied companies

collected during preclinical development. The first phase of clinical trials refers to testing new drug products or treatments on a small number of subjects to evaluate safety and dosing. Phase 2 consists of further evaluation of a drug's safety and efficacy on a larger population. In Phase 3, the drug's effectiveness, side effects and safety on a larger, statistically significant group of patients versus an active control (e.g. placebo or current standard of care) is conducted (Table II).

In the studied categories, finance-related assets of the firms include revenue, net income, cash and retained earnings. Moreover, organizational-related assets include the employees, CEO tenure and number of the board of directors' members, year of foundation and year of IPO. Finally, product-related assets include the number of products in each stages of development.

	Definition
Enterprise value	The market capitalization of a company is simply its share price multiplied by the number of shares a company has outstanding. Enterprise value is calculated as the market capitalization plus debt, minority interest and preferred shares, minus total cash and cash equivalents
Market capitalization	The value of a company that is traded on the stock market, calculated by multiplying the total number of shares by the present share price
Revenue	Income, especially when of a company or organization and of a substantial nature
Net Income	Net income (NI) is a company's total earnings (or profit); net income is calculated by taking revenues and subtracting the costs of doing business such as depreciation, interest, taxes and other expenses
Retained earnings	Retained earnings refer to the percentage of net earnings not paid out as dividends, but retained by the company to be reinvested in its core business, or to pay debt. It is recorded under shareholders' equity on the ba lance sheet
No of employees	# of Employees
CEO tenure	Number of years since the last CEO change
No of board members	Number of people in the board of directors
Year founded	Company establishment year
IPO	An IPO is the first time that the stock of a private company is offered to the public. IPOs are often issued by smaller, younger companies seeking capital to expand, but they can also be done by large privately-owned companies looking to become publicly traded
# of clinical and marketed products	Total number of products in phase 1, 2, 3 and commercial
Total # of products	Total number of products in program area, discovery, preclinical, phase 1-3, commercialized

Table II.
Variable definitions

We evaluated relationships between the enterprise value of the studied firms with these financial, organizational and product attributes in the disruptive biopharma sub-sector of rare diseases with the following hypotheses:

H1. Revenue of rare-disease-focused biotech companies is positively correlated with their enterprise value.

H2. The net income of rare-disease focused biotech companies is positively correlated with their enterprise value.

H3. Retained earnings of rare-disease focused biotech companies is positively correlated with their enterprise value.

H4. Number of employees in rare-disease focused biotech companies is positively correlated with their enterprise value.

H5. Length of CEO tenure in rare-disease focused biotech companies is positively correlated with their enterprise value.

H6. Number of board members in rare-disease focused biotech companies is positively correlated with their enterprise value.

H7. The establishment year of rare-disease focused biotech companies is positively correlated with their enterprise value.

H8. Years since the IPO of rare-disease-focused biotech companies is positively correlated with their enterprise value.

H9. Number of products in clinical or commercial stages in rare-disease-focused biotech companies is positively correlated with their enterprise value.

H10. Number of total products (From discovery to commercial stages) in rare-disease focused biotech companies is positively correlated with their enterprise value.

To test these hypotheses, we used regression analysis (with 95 per cent confidence) with the dependent variable "Enterprise Value" against independent variables in each hypothesis with respect to correlation (r), p-value (p) and R-squared (R^2) (Eisenberg *et al.*, 1998; James and Williams, 2012). Statistical modeling, in this case regression analysis, helps this study by more accurately estimating different correlations between different variables. Regression analysis has been used in other research and industries which have different mixes of similar business (James and Williams, 2012). Correlation is the degree which two metric variables are related in a linear manner.

In this case, (0-(-) 0.3 is considered as weak correlation; (-) 0.3-(-) 0.5 is considered medium correlation; and (-) 0.5-(-) 1.0 is considered as strong correlation. Negative correlations mean that an increase or decrease in the independent variable would result in the decrease or increase in the dependent value. The p-value shows the significance ($p < 0.05$) of the hypothesis. This means that if the p-value for each of the tests is >0.05 we reject the hypothesis. However, if the p-value is <0.05, we accept the hypothesis and consider the underlying assertion valid. In addition, R^2 refers to the percentage of "Enterprise Value (EV)" that can be explained by different independent variables. In other words, R^2 determines the proportion of the variance in EV that can be predicted using the tested independent variable. Finally, the non-standardized coefficient shows the amount of unit changes in the "Enterprise Value" with respect to changes in each independent variable. Also, although there is not a requirement for observed data to be normally distributed, errors are assumed to be normally distributed.

5. Results and discussion

Our results in Table III indicate that "Revenue", "Retained Earnings", "Number of Employees", "Number of Board Members", "IPO", "Clinical/Marketed Products" and "Total Number of Items in the Pipeline" had predictive power of "Enterprise Value" for the studied rare disease companies. In terms of correlation, the number of employees and revenue are most correlated with the enterprise value with 0.96 and 0.91 correlations respectively followed by number of products in clinical/market phase with a 0.73 correlation. A −0.50 correlation between IPO and enterprise value means that an older IPO date can result in higher enterprise value (i.e. experience tends to be cumulative). Our results indicate that a new drug added to the company's clinical/marketed portfolio can lead to about 1.3 billion units increase in "Enterprise Value" (i.e. depth and breadth of portfolio is accretive); while having an extra employee may potentially lead to $8.4m in enterprise value (i.e. adding team members in knowledge-based industries tends to add value). Finally, R^2 values for number of employees (93 per cent) and revenue (82 per cent) are correlated with EV. On the other hand, the effect of "Net Income", "CEO Tenure", and "Year Founded" on "Enterprise Value (EV)" are insignificant (p-values >0.05).

	Revenue	Net Income	Retained earnings	No of employees	CEO tenure	Board members	Year founded	IPO	Clinical-marketing	Total pipeline
Correlations	0.91	*0.18*	0.73	0.96	*0.02*	0.56	*−0.20*	−0.50	073	0.55
R Square	0.82	*0.03*	0.53	0.93	*0.00*	0.31	*0.042*	0.25	0.53	0.30
Coefficient	8.43	*6.33*	8.44	8.40	*39.58*	2354.90	*−116.34*	−444.64	1300.70	628.12
p-value	0.00	*0.40*	0.00	0.00	*0.90*	0.00	*0.33*	0.01	0.00	0.00

Table III.
Regression results for all companies (enterprise value as dependent value)

These results mean that we reject *H2, H5* and *H7*, while we fail to reject the other hypotheses as those independent values predicted enterprise value. While we fail to reject 7 out of 10 hypotheses, only four are strongly correlated with enterprise value with correlation values closer to 1.0 (two with correlation of higher than 0.9).

We next analyzed rare disease companies by size based on their market capitalization. Using the Biocentury (2017) database, we categorized companies "small" firms as less than $1bn market capitalization; "mid-sized" companies with market capitalizations of >$1bn to <$10bn; and "large" companies as >$10bn of market capitalization. As only 2 of the 24 studied companies fall under large cap category, large and medium cap companies are merged. Based on the data in Table IV, "Revenue" and "Number of employees" are still highly correlated with "Enterprise Value", as well as "Retained Earnings", "IPO", "Clinical/marketed products", and "Number of board members". However, *H10* is added to the rejected hypotheses compare to the test with all the companies. Finally, it can be seen that, based on R^2, a significant amount of EV can be explained by number of "Employees", "Retained Earnings" and "Revenue".

Finally, the analysis for small cap companies shows that the only correlation we fail to reject is the "Net Income" with a −0.77 correlation with the "Enterprise Value" (because of the fact that most of the studied companies are development stage with negative net incomes). This indicates that it is harder to impute different variables to EV when companies have smaller capitalization values as shown in Table V. The errors of the linear regression calculations were further controlled in terms of normalcy pointing to valid hypothesis testing. As for the observed data, contrary to the errors, they were not normally distributed because of the fact that only a small percentage of studied companies have the most value in terms of enterprise value, revenue, and number of employees among other things resulting in creation of outliers (normalcy assumption for the observed data is not required for linear regression, including *t*-test and ANOVA).

The summary of the results of hypotheses in each scenario and descriptive statistics for the studied companies is shown in Table VI.

The scatter plots for selected independent variables compared to the enterprise value for the studied company are also shown in Figure 4.

6. Conclusion

Biopharma companies have to constantly deal with intense financial, competitive, regulatory, technological, intellectual property and market fluctuation pressures. Because of these high rates of change, competitive advantage can be precarious and short-lived. Hence, the constant morphing and management of intangible assets and resources (i.e. sensing, seizing and transforming) is crucial to success and survival. Numerous examples of dynamic capabilities in technology-based firms highlight the need to respond to market price changes, acquisition to reconfigure resources, product innovation for organizational renewal, organizational structure reconfiguration and resource divestment (Helfat, 1997; Karim and Mitchel, 2000; Danneels, 2002; Moliterno and Wiersma, 2007; Ambrosini and Bowman, 2009; Lawson and Samson, 2001; Rothaermel and Hess, 2007).

To attain these capabilities and build value, it is important for high-tech firms to attract expertise (i.e. employees in different levels of the organization such as researchers and board of director members) to steer company toward competitive advantage and commercial success. Moreover, the aggregation of skilled and innovative employees can lead the development of new product innovation and guide it towards a more versatile and efficient product pipeline. The know-how and experience that the workforce can bring (especially in

	Revenue	Net Income	Retained earnings	No of employees	CEO tenure	Board members	Year founded	IPO	Clinical-marketing	Total pipeline
Correlations	0.9	*0.44*	0.90	0.96	*−0.14*	0.68	*−0.32*	−0.67	0.74	*0.49*
R^2	0.82	*0.20*	0.82	0.92	*0.02*	0.46	*0.10*	0.45	0.55	*0.24*
Coefficient	8.07	*15.61*	9.68	8.56	*−303.40*	3798.31	*−254.80*	−726	1699.34	*576.59*
p-value	0.000	*0.16*	0.00	0.00	*0.66*	0.021	*0.33*	0.02	0.00	*0.12*

Table IV.
Regression results for big–medium companies (enterprise value as dependent value)

	Revenue	Net Income	Retained Earnings	No of Employees	CEO Tenure	Board Members	Year Founded	IPO	Clinical-Marketing	Total Pipeline
Correlations	−0.28	*−0.77*	−0.45	−0.21	*−0.09*	−0.33	*0.11*	−0.35	0.11	*0.41*
R^2	0.07	*0.60*	0.20	0.04	*0.01*	0.11	*0.01*	0.12	0.01	*0.17*
Coefficient	−0.77	*−4.93*	−0.67	−0.94	*−6.57*	−66.98	*2.68*	−13.50	16.16	*44.06*
p-value	0.37	*0.00*	0.12	0.48	*0.76*	0.26	*0.70*	0.25	0.70	*0.16*

Table V.
Regression results for small companies (enterprise value as dependent value)

bigger companies) can be seen as a cumulative bolstering factor in leveraging dynamic capabilities which can be recognized, understood, and transformed to align with company goals and commercial success (i.e. increasing returns in enterprise value). In other words, the implications for technology managers are that their role is to manage not only the financial aspects of the technology but also human resources, asset configuration and strategic alliances efficiently toward faster and better innovation. The implication for technology-based companies is that people and location may have a significant impact on aggregating dynamic capabilities and increasing enterprise value. Strong dynamic capabilities can be formed with the accumulation of experience, articulation and codification of knowledge, and an adaptive ability to change the way they solve problems as the environment transforms (Zahra and Sapienza, 2006). In the case of biopharma firms, more efficient, prolific, and versatile staff can lead to better new product development and a more efficient research and development pipeline.

The disruptive genomics revolution provides rare disease-based companies the opportunity to create significant value and upend the entire global biopharma industry from mass market to personalized medicine. Leveraging genomics and new technologies can guide biopharma firms to enhance product innovation and bolster their chances of attracting employee expertise, insightful boards of directors and management teams. Biopharma managers should be alert in sensing the opportunities, threats and resources followed by seizing them and reconfiguring them to fit their organization to gain and sustain competitive advantage.

In this study, 24 rare disease-focused biopharma companies were studied and several variables were tested with respect to enterprise value. The companies were analyzed as a group of rare disease firms, as well as by size. We found that variables such as number of employees, revenue, number of products in clinical/market stages and retained earnings are strongly correlated (in that order) with the enterprise value in rare disease-focused biopharma companies. These correlations seem to be weaker as a company's market capitalization size decreases, indicating that there tends to be an increasing return to scale. This study is limited by a small sample of the disruptive gene therapy sub-sector and may not be generalizable to other nascent technology-based industries. As an extension of this study, we would suggest comparing these results against the entire biotechnology industry as whole to better differentiate specialized rare disease companies.

Using a dynamic capabilities lens, this paper studied the impact of genomics generally and gene therapy specifically on the rare disease sector of the biopharmaceutical industry. This study found that increasing rates of cumulative returns depends on accumulating knowledge-based employees and expanding product portfolios of disruptive genomics-based technologies for treating rare diseases. Further, this study highlights the importance of building the capability and capacity to absorb expertise and accumulate knowledge for new product innovations and sustainable competitive advantage.

Table VI. Results of hypotheses in different scenarios

Type of company	Hypotheses which are not rejected
All	*H1, H3, H4, H6, H8, H9, H10*
Only large and medium	*H1, H3, H4, H6, H8, H9*
Only small	*H2*

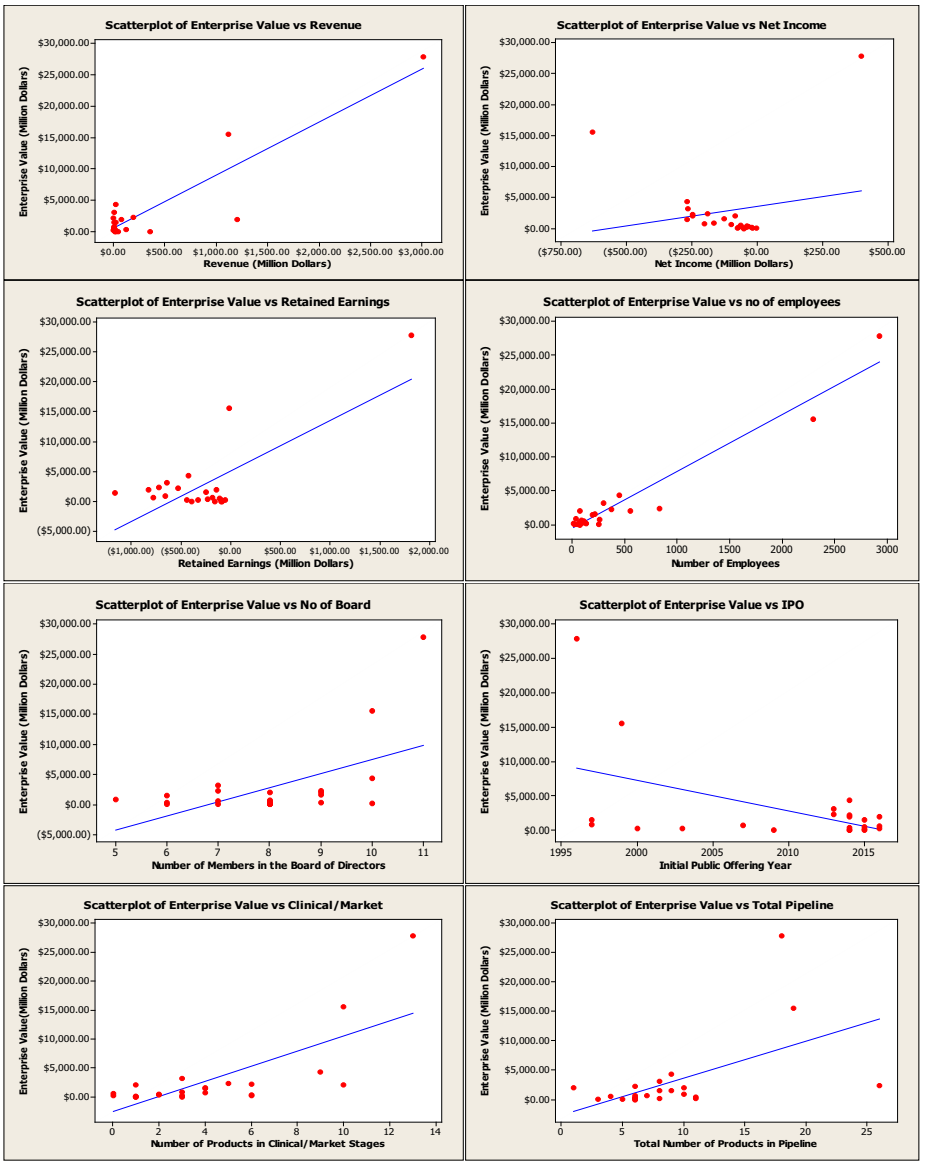

Figure 4.
Enterprise value curve estimations for different variable

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