

NEKTAR THERAPEUTICS STRATEGY REPORT



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EXECUTIVE SUMMARY

Nektar Therapeutics, (NASDAQ: NKTR) a clinical-stage biopharmaceutical company, was incorporated in California in 1990 and reincorporated in Delaware in 1998. The company, which develops therapeutics, is headquartered in San Francisco, CA but also has operations in Huntsville, Alabama and Hyderabad, India. Nektar had an initial public offering in 1994 and has been public ever since. The company is lead by CEO Howard W. Robin who has been with the company since 2007. The company provides a range of drug delivery technologies to aid pharmaceutical and biotechnology companies with their products, delivery, franchises, and product pipelines. The company falls under the healthcare sector and more specifically the biotechnology and drugs industry.

Nektar uses their proprietary PEGylation and advanced polymer conjugate technology platforms to improve the effectiveness of their drugs. The current pipeline is made up of drug candidates across many therapeutic areas including anti-infective, anti-viral, immunology, oncology, and pain. Through partnerships with other biopharmaceutical companies, Nektar currently has ten approved products; along with these approved products, the company has a dozen other drugs in their research and development (R&D) pipeline; these include drugs in preclinical phases such as NKTR-171 all the way to drugs, which are applying for FDA and EMA approval, such as Naloxegol (NKTR-118). Collaboration with other biopharmaceutical companies has been and for the foreseeable future will be a key part of Nektar's business strategy; these partnerships with major pharmaceutical companies have greatly aided in financing the development of new products. For example, the company's development deal with AstraZeneca made in 2009 netted them \$125 million up-front and also gives them the opportunity to earn an additional \$1.5 billion in milestone payments;¹ currently, they are also looking for a collaborative partner for their NKTR-102 candidate, in order to guide it through regulatory filings and commercialization in three separate clinical trials for breast, colorectal, and ovarian cancers.²

In the past, Nektar has struggled to be profitable never having generated a profit and posting a net income of -\$171.9 million in 2012. Their current business strategy in attempt for profitability

¹ Nektar Therapeutics 10-K 2012

² Hoover's Nektar Company Report



include four key element: advance their proprietary clinical pipeline of drug candidates through various stages of clinical development, ensure future growth of their proprietary pipeline to maintain a diverse pipeline of new drug candidates building on the current pipeline, enter into strategic and high-value partnerships to bring certain of drug candidates to market, and lastly continue to build an intellectual property estate in the field of PEGylation and polymer conjugate chemistry.

The company seems to be in position to establish profitability in the future with their extensive R&D pipeline. For the near term, Nektar must focus on pushing AstraZeneca to file a New Drug Application (NDA) for Naloxegol. The approval of this drug candidate will go a long way in creating revenues for Nektar in milestone payments. They should also focus on creating a brand for themselves and maintaining current partnerships while continuing to look for new partnerships on order to attain capital to continue research.



COMPANY BACKGROUND

Nektar Therapeutics utilizes their PEGylation and advanced polymer conjugate technology platforms in order to deliver drugs. They have a strong research and development department with a number of potentially high-value therapeutics in area including oncology, pain, anti-infective, and immunology. The company has many drugs that are in clinical studies as well as ten approved products in the US and/or Europe through partnerships with biopharmaceutical companies such as Affymax, Amgen, MAP Pharmaceuticals, Merck, Pfizer, Roche, and UCB Pharma. Our drug candidates are designed to improve the overall benefits and use of a drug for patients by improving the metabolism, distribution, pharmacokinetics, pharmacodynamics, half-life and/or bioavailability of drugs.

Polymer chemistry is a science focused on the synthesis or bonding of polymer architectures with drug molecules to alter the properties of a molecule when bonded with polymers. PEGylation is a technology based on repeating unites of polyethylene glycol (PEG); PEG is a water-soluble, amphiphilic, nontoxic, and nonimmunogenic compound. The primary use of PEGylation has been to improve properties of large molecules, but it can also attach to smaller molecules in some cases without affecting the functionality of the drug. This technology attaches the polymer PEG to peptides, proteins, and antibody molecules, which alters the physiochemical properties of the molecule. Practically, this helps improve the safety and efficiency of many therapeutics. By increasing the molecular weight of a molecule, PEGylation can improve drug solubility, reduce dosage frequency without reducing efficacy and potentially reducing toxicity, extend circulating life, increase drug stability, and prevent degradation of the molecule with which PEG attaches.

Nektar Therapeutics' objective is to advance lead drug candidates through various stages of clinical development. To accomplish this objective, they have significantly expanded and added expertise to their internal preclinical, clinical development, and regulatory departments over the past five years. Part of their development strategy is to reduce the time and risks associated with drug development by abstracting safety and efficacy strategies from approved drugs. While developing drugs, they maintain a breadth of focus by working on a diversity of new drug candidates within their PEGylation technology platform.



When developing a new drug, they choose one of three routes to take, which is decided on a drug candidate-by-drug candidate basis; they either commercialize the drug on their own, seek a partner, or pursue a combination of these two approaches during a drug's development (e.g. Preclinical, Phase 1, 2, and 3). The research/preclinical phase is the earliest stage of development in which a drug candidate is being studied by way of vitro studies and/or animal studies. In phase 1, the drug candidates are tested in healthy subjects for safety. Phase 2 tests drug candidates in clinical trials to establish dosing and efficacy. Phase 3 trials are large-scale trials following successful trials in phase 2. During phase 3, Nektar seeks to obtain regulatory approval in order to sell the drug on the market, which it can begin to do once the application has been approved. When they seek a partner during one or more of the development phases, their strategy is to collaborate with leading pharmaceutical and biotechnology companies to fund further clinical development, manage the global regulation process, and market and sell the drug in certain geographies.

In 2008, two Nektar drugs, NKTR-102 and NKTR-118 were named to R&D Directions '100 Greatest Investigational Drugs' list. To date, Nektar and their partners have produced ten products that have been approved in the U.S. and/or Europe and are used by medical professionals and patients around the globe. Below are two table summarizing their current approved drugs and drug candidates:



Products	Status	Indication	Partner	Therapeutic Area
OMONTYS® (peginesatide)	Approved U.S.	Anemia in chronic kidney disease (CKD)	 AFFYMAX.	Nephrology
Cimzia®	Approved in U.S.	Crohn's disease Rheumatoid Arthritis		Immunology
MIRCERA®	Approved in EU/U.S.	Anemia in chronic kidney disease (CKD)		Nephrology
Neulasta®	Approved	Neutropenia		Oncology
PEGASYS®	Approved	Hepatitis C		Immunology
PEG-INTRON®	Approved	Hepatitis C		Immunology
DEFINITY® Vial	Approved	Diagnostic		Surgical/Imaging
DuraSeal®	Approved	Cranial Durant Sealant		Surgical/Imaging
Somavert®	Approved	Acromegaly		Immunology
Macugen®	Approved	Wet age-related macular degeneration		Ocular

Table 1: Currently Approved Drugs³

³ “Approved Products” – www.Nektar.com



Drug Candidate/Program	Target Indications	Status(1)
Naloxegol (orally available peripherally-acting mu-opioid receptor antagonist)	Opioid-induced constipation	Completed Phase 3 (Partnered with AstraZeneca AB)
Etirinotecan pegol (next-generation topoisomerase I inhibitor)	Metastatic breast cancer	Phase 3
BAY41-6551 (Amikacin Inhale, formerly NKTR-061)	Gram-negative pneumonias	Completed Phase 2 (Partnered with Bayer Healthcare LLC)*
Etirinotecan pegol	Platinum-resistant/refractory ovarian cancer	Completed Phase 2
Etirinotecan pegol	Second-line metastatic colorectal cancer in patients with the KRAS gene mutation	Phase 2
NKTR-181 (orally-available mu-opioid analgesic molecule)	Moderate to severe chronic pain	Phase 2
Etirinotecan pegol (in combination with 5-Fluorouracil/leucovorin)	Metastatic colorectal cancer	Completed Phase 1
NKTR-192 (orally-available mu-opioid analgesic molecule)	Acute pain	Phase 1
Naloxegol fixed-dose combinations (opioid/NKTR-118 combinations)	Chronic pain without constipation	Research/Preclinical (Partnered with AstraZeneca AB)
NKTR-171 (orally-available peripherally-acting sodium channel blocker)	Neuropathic pain	Research/Preclinical
NKTR-214 (cytokine immunostimulatory therapy)	Oncology	Research/Preclinical

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Table 2: Nektar's R&D Pipeline⁴

Over the company's history, Nektar has partnered with AstraZeneca, Bayer Healthcare LLC, Affymax, MAP Pharmaceuticals, Inc., subsidiaries of Baxter International, Amgen, Inc., F. Hoffmann-La Roche Ltd, Pfizer, Merck, Valeant Pharmaceuticals International, Inc., and UCB Pharma while working on drug development. On December 31, 2008, assets related to their pulmonary business and associated technologies were sold to Novartis for \$115 million. Revenues are accrued from collaboration agreements with their partners. UCB Pharma, Roche, and Affymax represented 30%, 23%, and 11% of Nektar's revenue, respectively, for 2012.⁵

At year-end 2012, Nektar employed 433 people, 325 of which were involved in research and development. They have 80 employees based in India. In 2006, Nektar was the 21st largest biotechnology company worldwide as ranked by annual revenue, for which Nektar made \$217.7 million in revenue for 2006.

⁴ "R&D Pipeline" – www.Nektar.com

⁵ Nektar Therapeutics 10-K 2012



FINANCIAL ANALYSIS

Overview

With a market capitalization of just \$1.27 billion, Nektar is much smaller than the giant players in the biotechnology and drug industry that it considers competitors. To overcome this size difference, Nektar often partners with larger drug companies for distribution and commercialization. However, their core business and products are similar enough to these larger companies that it is still useful to compare Nektar's financials to the industry leaders and averages. Thus far, Nektar, in collaboration with their partners, has developed and brought to market ten approved products. In addition to the ten approved products, they have a long list of drugs and technologies that are in various stages, ranging from preclinical development phase to phase 3 of clinical trials. The success of these products that are still under development and have not yet reached market will dictate the financial success of the company over the next few years.⁶

Profitability & Growth

Nektar's ten already-approved products have been the primary source of revenue for the company, and the proprietary drugs and technologies that are currently in the development and testing stages are poised to drive revenue in the coming years. As a result of the upfront lump payments Nektar receives from many of their licensing and collaboration agreements, there can be considerable variation in the timing of receipt of payments, and therefore significant variation in revenue from period to period. Accordingly, the large changes in year-to-year revenues, particularly the sharp decrease from 2010 to 2011, does not indicate a contraction of the company, but instead reflects the nature of Nektar's fee payments.⁷

In order to continue development and testing of new drugs and technologies, Nektar has committed a significant amount of capital to funding these projects, as is evidenced by the large and increasing research and development expenditures over the past few years. Nektar's management states in the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of the company's recently published 2012 10-K report that they are committed to investing in the ongoing development programs of drugs in all different stages of development, as

⁶ "Investor Relations" - Nektar.com

⁷ Nektar Therapeutics 10-K 2012



well as starting new development projects. Even though the drugs and technologies that are currently in the beginning stages of the process will not produce revenues in the immediate future due to the many required years of testing and clinical trials, management recognizes the importance of these products for the future wellbeing of the company: “While the late stage clinical development programs are key elements of the future success of our company, we believe it is critically important that we continue to make substantial investments in our earlier-stage drug candidate pipeline.”⁸

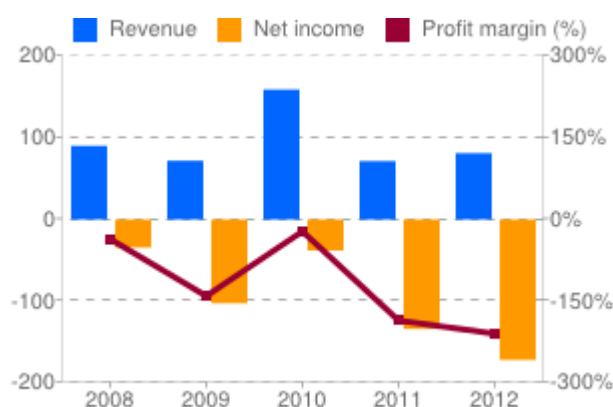


Figure 1: Nektar Revenues, NI, and Profit Margin from 2008-2012 (in Millions)⁹

Nektar’s high R&D spending has far outpaced their revenue from products and partnerships over the years, so the company has been far from profitable. In fact, the growing R&D costs have caused net income to be increasingly negative over the past three years, with the company losing \$171.85 million in 2012. Nektar has reported net losses for each of the past five years and has had inconsistent revenue over this period. However, due to the nature of developing drugs as a business, it is reasonable for a company in this industry to have significant losses while they spend money to develop products, with profitability following once these drugs reach market. The ultimate success of Nektar or any other with this plan depends largely on the company’s ability to develop drugs and drug-related technologies that successfully earn approval from the necessary authorities and also have large commercial appeal.

⁸ Nektar Therapeutics 10-K 2012

⁹ Reuters.com



To determine Nektar's prospects for the near future, one can look at Nektar's upcoming product candidates. In particular, Nektar's most advanced drug candidate, naloxegol, has completed its Phase 3 clinical studies and is in position to be a significant source of revenue for the company in the near future. The drug, which treats opioid-induced constipation (OIC), is the closest to completing the drug approval process out of all of Nektar's current drug candidates. Nektar has entered into a licensing agreement with AstraZeneca for naloxegol, giving AstraZeneca exclusive right to development and global commercialization of naloxegol and naloxegol combination products. The results of the naloxegol development program and subsequent commercialization, which are now run by AstraZeneca, have significant implications for the financial condition of Nektar. Nektar stands to receive up to \$95 million when the drug has passed certain filing milestones and up to \$140 million when the drug has reached various commercial launch milestones. In announcements made on November 12, 2012 and February 26, 2013, AstraZeneca revealed positive results from two Phase 3 efficacy and safety clinical trials and from a long-term safety study. AstraZeneca has declared plans to submit filings to the U.S. and E.U. in Q3 of 2013. If these submissions receive approval from both regulatory authorities, Nektar will be entitled to \$95 million from AstraZeneca. This revenue alone would exceed Nektar's 2012 and 2011 revenues. Nektar's other product candidates are further from reaching market, providing greater uncertainty about the likelihood of approval and the potential revenues they would drive.¹⁰

Liquidity & Solvency

Barring significant increases in the costs of Nektar's current drug development programs, which management has noted is a possibility due to the unpredictable nature of drug development and clinical trials, current estimates predict that solvency will not be an issue for Nektar in 2013. The company entered 2013 with over \$300 million in cash, cash equivalents, and investments in marketable securities and approximately \$150 million in debt, and as of the 2012 year-end had enough working capital to fund their business plans for at least the next twelve months.¹¹

¹⁰ Nektar Therapeutics 10-K 2012

¹¹ Nektar Therapeutics 10-K 2012



Nektar has a solid current ratio of 4.1, which is slightly below the biotechnology and drugs industry average of 4.68, but well above the healthcare sector average of 2.09.¹² Although this current ratio supports management's declaration that the company has enough capital for the 2013 year, they have admitted that if costs are higher than expected or anticipated revenues take longer to come to fruition, they will likely need to seek additional financing for operations beyond 2013.

DuPont Analysis

To analyze Nektar's return on equity (ROE) of -140.39, we can break down the ROE into three components, profitability operating efficiency, and financial leverage, in order to examine where we they can improve on this statistic.

- 1) We see that the profit margin for the last year is -212%, calculated by:

$$\text{Net Income/Sales} = -\$171.9 \text{ million} / \$81.2 \text{ million} = -212\%$$

- 2) We see that the asset turnover ratio is 0.16, calculated by:

$$\text{Sales/Total Assets} = \$81.2 \text{ million} / \$497.8 \text{ billion} = 0.16$$

- 3) We see that the equity multiplier is 10.6, calculated by:

$$\text{Total Assets/Total Equity} = \$497.8 \text{ million} / \$47 \text{ million} = 10.6$$

DuPont Analysis of Nektar and Competitors ¹³				
	NKTR	BMJ	ENZN	Industry Median
Profit Margin (ttm)	-211.67	14.19	-6.53	83.07
Asset Turnover (ttm)	0.16	0.51	0.16	0.42
Equity Multiplier (ttm)	10.6	1.83	1.94	-
Return on Equity (ttm)	-140.39	13.24	-2.03	11.69

¹² Reuters.com—Nektar Therapeutics Financials

¹³ Hoovers.com: Nektar Therapeutics – Competitive Landscape



Nektar's significant net losses over the past twelve months have been the major contributor to the company's hugely negative return on equity of -140.39%. The company has been pouring money into their development and clinical trial programs, but Nektar will not realize the revenues from these investments until the products are successfully approved and reach market. Since Nektar only has a handful of products currently on the market, with the majority of their revenue potential still in testing, sales have been relatively low recently, causing the company to have a highly negative profit margin and a low asset turnover. The table above lists competitors Bristol-Myers Squibb Co. (BMY) and Enzon Pharmaceuticals Inc. (ENZN), but comparisons to other companies in the industry provide only minimal insight. Since companies must invest considerable capital to develop and test new products and receipt of revenue is delayed until product approval, firms ratios for a given period are highly dependent on where in the development, test, launch-to-market cycle they currently stand. The majority of Nektar's products have not yet reached market, which has depressed the company's profit margin, asset turnover, and return on equity.

Stock Performance



Figure 2: Nektar vs S&P 500 Trailing Twelve Months¹⁴

Seen above, Nektar Therapeutics, NASDAQ ticker NKTR, has performed well year-to-date as well as the trailing twelve months (TTM) in comparison to the Biotechnology and Drugs Industry and the S&P 500. Since Nektar is a clinical-stage biotechnology company that aids pharmaceutical

¹⁴ Finance.yahoo.com



companies and does not market their own drugs, we looked more specifically at the biotechnology industry.

Direct Competitor Comparison					
	NKTR	BMJ	ENZN	GSK	Industry
Market Cap:	1.20B	67.25B	167.13M	119.26B	105.24M
Employees:	433	28,000	43	99,488	53.00
Qtrly Rev Growth (yoy):	0.34	-0.23	0.06	-0.03	0.18
Revenue (ttm):	81.19M	17.62B	41.73M	42.48B	14.28M
Gross Margin (ttm):	0.63	0.75	1.00	0.71	0.70
EBITDA (ttm):	-125.02M	5.66B	11.38M	14.75B	-6.15M
Operating Margin (ttm):	-1.72	0.27	0.17	0.29	-1.01
Net Income (ttm):	-171.85M	1.96B	-2.78M	7.34B	N/A
EPS (ttm):	-1.50	1.16	-0.06	2.94	-0.12
P/E (ttm):	N/A	35.41	N/A	16.79	18.96
PEG (5 yr expected):	-0.67	2.62	N/A	3.62	N/A
P/S (ttm):	15.59	3.85	4.14	2.75	9.78

Table 3: Nektar vs Competitors

Looking at Enzon Pharmaceuticals, Inc., NASDAQ ticker ENZN, their main public competitor, we can see that NKTR has fared much better in the trailing twelve months. The closing price of a stock was \$11.15 as of April 18, 2013; though the price has been very volatile in the trailing twelve months with a 52-week low of \$5.65 and high of \$11.21, NKTR has seen an upward climb since the low on November 14, 2012. We should note that due to the nature of the biotechnology industry the volatility should be expected caused by the status of their drug pipeline; we anticipate more unpredictability in the price with five drugs in the final clinical stage waiting on FDA approval.



COMPETITIVE ANALYSIS

Market Definition

The biotechnology and drug industry in the US can be broken up into the two obvious sectors, biotechnology and drug. As Nektar focuses on the development of drugs with their proprietary technology, not on the commercialization and marketing of drugs, we looked further into the biotechnology portion of this industry. In defining Nektar's competitors, we examined companies that focus on the drug development rather than the commercialization and marketing of drugs. For the purpose of this analysis, we must also focus mainly on small or med cap companies that fall under this industry such as Enzon mentioned above. Larger companies such as Pfizer (NYSE:PFE), which has a market capitalization of over \$200 billion, must be also be analyzed but cannot be compared as a direct competitor especially as Nektar have partnerships with many of these mega cap companies which marketing and commercializing their drugs.

Internal Rivalry	High
New Entry & Exit	Low
Substitutes	Low
Buyer Power	Low to Moderate
Supplier Power	Low → Moderate

Internal Rivalry – High

As the quintessence of biotechnology/pharmaceutical companies is the discovery of drugs and delivery process, which has an extremely high cost for research and development, the rivalry among companies is extremely high. It is crucial for firms to continually seek new treatments and begin the highly regulated clinical trial process for groundbreaking drugs, as revenue from these drugs is vital to the survival of each company; for this reason, each competitor must rush to file a New Drug Application with the governing agency, Food and Drug Administration (FDA) in the US and European Medicines Agency (EMA) in the European Union for approval to sell the drug on the market. Creating novel compounds that successfully treat a condition can be very lucrative, as



patenting these drugs will usually lead to a monopoly in treatment of the condition for up to 12 years.¹⁵

As profitable as these new medicines can be, the rejection of a drug by the central agency can also be massive setback for the company due to a huge financial loss from research costs. In order to embrace these obstructions, firms must have a large portfolio of drugs and technologies to strengthen the R&D pipeline. Companies that focus on creating new compounds and deliverance methods must also compete with the firms that concentrate on producing generic drugs; as these firms produce drugs that are not protect by patents, they do not have large R&D spending and are able to undercut the brand drugs to gain a profit while demolishing revenues for the companies that originally developed the drugs.

Entry & Exit - Low

Barriers to entry are very high in the biotechnology and drug industry; two of the main reasons are the high costs of research and development and the amount of time required for a drug to go through clinical trials and obtain approval by the governing agency; hence, this is a capital-intensive industry which has very high startup costs and delayed revenues. Well-developed companies in this industry have many drugs on the market, which fuel the research and development of new drugs and technologies; by having a large drug R&D pipeline with drugs in all clinical trial stages, companies can compensate for the delay or even the denial of a NDA with other pipeline products. Startups that cannot get an approval of enough drugs to continue this cycle of marketing drugs to augment seed money for future R&D will be bankrupt quickly.

¹⁵ <http://healthreform.kff.org/timeline.aspx>

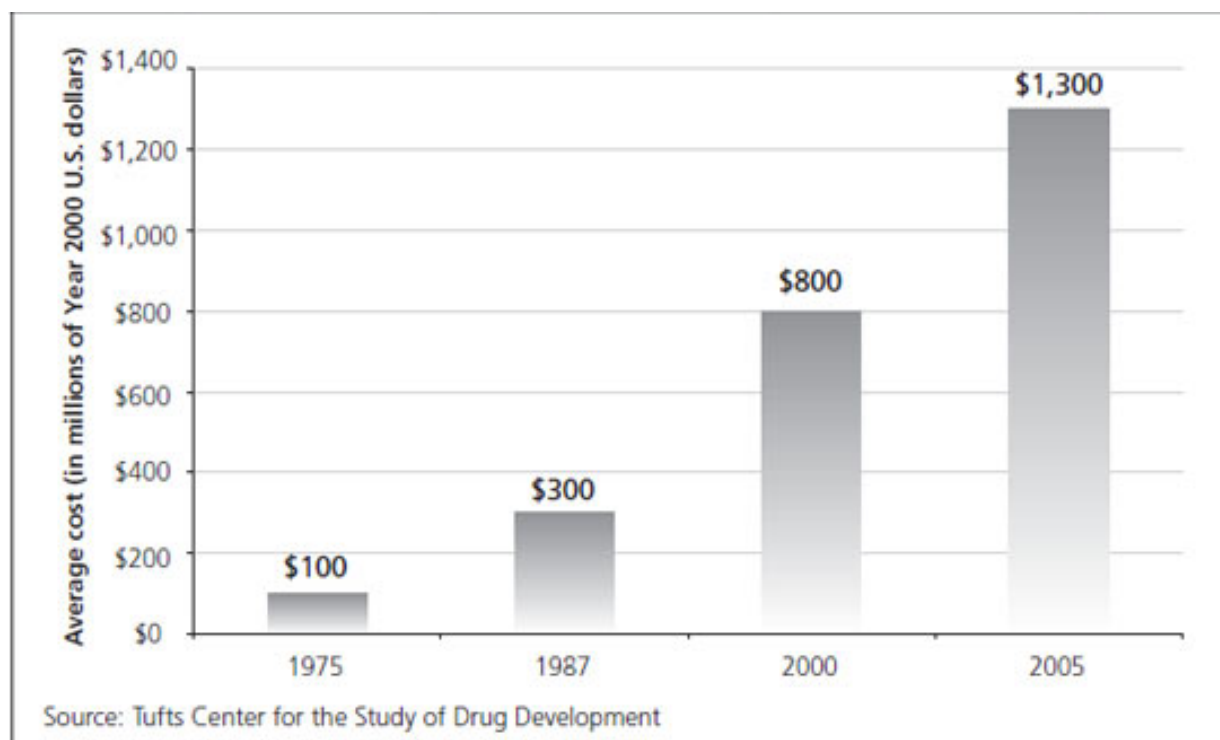


Figure 3: Average Cost to Develop One Drug¹⁶

Function	Dollars (xMM)	Share of Total	Probability of FDA Approval
Prehuman/preclinical	\$11,717.4	28.6%	8%
Phase I	\$ 3,752.9	9.2%	21%
Phase II	\$ 7,123.7	17.4%	28%
Phase III	\$16,300.1	39.8%	58%
Approval	\$ 2,046.9	5.0%	90%
Total R&D up to FDA approval	\$40,941.0	100.0%	
Phase IV	\$ 5,302.7	13.0%	
Uncategorized	\$ 197.8	0.5%	

Source: PhRMA Annual Member Survey, 2011; DiMasi et al., J Health Econ 22(2003):151-85

Table 4: R&D by Function, PhRMA Member Companies, 2009¹⁷

Figure 3 shows the high costs of R&D with the production of one drug averaging over \$1.3 billion. With R&D costs potentially as high as \$41 billion (Table 5), the failure of a drug can be devastating for a new entrant. Furthermore, exiting the industry is also costly having to find a buyer willing to purchase each of the drugs in the R&D pipeline as well as the already approved drugs.

¹⁶ http://www.manhattan-institute.org/html/fda_05.htm

¹⁷ http://www.manhattan-institute.org/html/fda_05.htm



Substitutes & Complements - Low

The threat of substitutes is the lowest among the Porter Five Forces. With the ability for biotechnology and drug companies to patent their compounds and deliverance technologies, firms are able to protect their revenues from brand drugs and technology platforms. Various treatments for the same problem, which differ in delivery method, will compete for the same market as substitutes. As mentioned in Internal Rivalry, most of the substitute competition occurs when patents for the novel drug and delivery technology platforms expire; the companies that solely create generic drugs and undercut the price of brand drugs greatly undermine the drug originators' revenues. Most products created by firms in the biotechnology and drug industry do not have compliments, as they are typically new treatments or innovative technology.

Supplier Power – Low to Moderate

With a low number of new entrants, suppliers do not continually have new customers that require their products when for all inputs from production equipment to biochemical raw goods; as there is little differentiation in most inputs necessary for research and development and there exist over 100 suppliers, suppliers have a low bargaining power on biotech or drug companies.¹⁸ Firms that provide special orders, advance technology, or special manufacturing understandably have greater bargaining power; some also have greater supplier power when they have a significant influence in the market, which make it difficult for members of the industry to switch to other suppliers when threatened by a price increase.

Buyer Power – Low but Increasing

The buyers, including the patients, hospitals, and pharmacies, currently have low buyer power in our defined market, as there exist few if any substitutes and these drugs are at times necessities for life. Buyers especially have limited bargaining power as they must get the drug prescribed to them and once they start a drug regimen it is difficult and sometimes dangerous to switching drugs. Buyers do have strong bargaining power whenever they purchase large volumes (i.e. hospitals) or when products become standardized after patents expire (i.e. generic drugs)

¹⁸ www.pharmaceutical-industry.info



Buyer's bargaining power is increasing with the implementation of the Patient Protection and Affordable Care Act (PPACA) or commonly called Obamacare. Obamacare is aimed at increasing health insurance coverage rates in the US and, more importantly, reducing the overall costs of health care. With the elimination of co-payments and deductibles for select "essential" health care insurance benefits, firms are getting squeezed of profits.¹⁹ Also, as Obamacare now requires insurances companies to cover all applicants at the same rates regardless of pre-existing conditions, the buyer, insurance companies in this case, will require cheaper pricing on drugs.²⁰ One of the most significant changes for biotech and drug firms like Nektar is that the FDA is now authorized to approve generic drugs after only 12 years of exclusive use down from the previous 20 years; this will have a greatly negative impact on the industry as it have depended on the fact that companies have exclusive use for 20 years in order to make up for the high costs of R&D.

¹⁹ "Essential Health Benefits" - www.healthcare.gov

²⁰ "ObamaCare Survives the Supreme Court" – www.theweek.com



SWOT ANALYSIS

SWOT Analysis	
Strengths	Weaknesses
· Robust Research and Development Activities with Many Drugs in Clinical Trials	· Substantial Losses in the Past
· Advanced Proprietary Technological Base/ Intellectual Property	· High R&D Costs
· Partnerships/Capital on Hand	
Opportunities	Threats
· Promising Product Pipeline	· Competitive Landscape
· Partnerships and Collaborations	· Uncertainties in R&D Outcomes from governing agencies
	· New Government Regulations /Difficult Pricing due to PPACA

Strengths

- **Robust Research and Development Activities with Many Drugs in Clinical Trials**

The biggest strength that Nektar has is their robust research and development activities. With a dozen drugs in their research and development pipeline, five of which are in the last clinical trial stage, they have a bright future ahead. Nektar has found three partnerships for four of the five late-stage programs with brand name pharmaceutical companies: Bayer, Baxter, and AstraZeneca; they project that these five drugs could generate over \$750 million per year in royalty income.²¹ This puts Nektar Therapeutics into a good position to achieve positive cash flow in the upcoming years.

Nektar and AstraZeneca are collaborating to create Naloxegol (NKTR-118), a treatment for opioid-induced constipation, and NKTR-119, an early stage drug development program with the goal of treating pain without the side effect of constipation that is

²¹ 31st Annual J.P. Morgan Healthcare Conference Presentation



associated with opioid therapy.²² Naloxegol, unlike BAX 885, Amikacin Inhale, Cipro DPI, and NKTR-102, has already completed phase 3 and needs to file a NDA in order to become a marketable drug; with more drugs in earlier stages Nektar's future is looking bright especially if they obtain the approval of a number of the previously mentioned late-stage programs.

- **Advanced Proprietary Technology Base and Intellectual Property**

Nektar's proprietary PEGylation and Advanced Polymer Conjugate Technology improves the effectiveness of drug deliverance. PEGylation is a technology based on repeating unites of polyethylene glycol (PEG). The primary use of PEGylation has been to improve properties of large molecules, but it can also attach to smaller molecules in some cases without affecting the functionality of the drug. This technology attaches the polymer PEG to peptides, proteins, and antibody molecules, which alters the physiochemical properties of the molecule. Other pharmaceutical companies utilize their proprietary technology for which Nektar receives royalties as they have exclusive rights to the technology. Having this advance technology base, Nektar can improve toxicity profile, better pharmacokinetics, extended half-life, and ease of synthesis with the antibody. In addition to these benefits, their technology improves the solubility of a drug enabling oral administration of originally parenterally-administered drugs, drugs that must be administered intravenously or subcutaneously. With more than 150 US and 500 foreign patents, their superior quality of drug administration that improve on the effectiveness and ease of drugs is one of the firm's main strengths.²³

- **Partnerships/Capital on Hand**

Entering the 2013 fiscal year with over \$300 million in cash, cash equivalence, and investments, Nektar project to have enough working capital to fund their business plans for the current fiscal year. Along with this capital, the company has many partnerships with large mega cap pharmaceutical companies such as Amgen, AstraZeneca, Pfizer, and Roche.²⁴ In one of their collaboration deals, AstraZeneca has agreed to be responsible for the

²² Product Pipeline – www.nektar.com

²³ Nektar Therapeutics 10-K 2012

²⁴ Our Partners – www.nektar.com



development, global manufacturing, and marketing of both Naloxegol and NKTR-119. In this agreement Nektar will receive royalty payments for achievement of certain regulatory milestones as well as commercial milestones. The large amount of cash will allow for the continuance of their research and development pipeline; Nektar is able to bring to market drugs that have enormous R&D costs by partnering with large companies with large amounts of capital for R&D.

Weaknesses

- **Substantial Losses in the Past**

As mentioned previously in the report, Nektar had a net income of -\$171.85 million during the fiscal year ending on December 31, 2012. The colossal amount lost in income is the main concern of Nektar. If we look back even further, we see that they had net incomes of -\$133.98 million, -\$37.94 million, and -\$102.52 million during years 2011, 2010 and 2009 respectively.²⁵ The substantially negative net income over the years is not sustainable even with over \$300 million in cash equivalents. Especially when Nektar has indebtedness of \$149 million, including \$125 million in senior secured notes, they must focus on changing this trend to become profitable.

- **High R&D Costs**

The main cause of the substantial losses in the past is due to the nature of the industry's high research and development costs. The high costs of developing a drug and putting it through clinical trials is inevitable. However, Nektar must minimize this cost in order to reduce the total spending and increase net income. As the average cost to develop one drug has been exponentially increasing (seen in Figure 3 above), Nektar must defray these costs through finding low-cost suppliers and creating sound drug candidates.

²⁵ Nektar Therapeutics 10-K 2012



Opportunities

- **Promising Product Pipeline**

As mentioned under Strengths, Nektar has a very promising Research and Development Pipeline along with current products already out in the market. With royalties from the ten products already out in the market, the company looks to augment their income greatly in the upcoming year with the five drugs programs that are in late clinical stages. The approval of these drugs has the possibility to make Nektar profitable with potentially over \$750 million per year in income. As Nektar has seven other programs in its pipeline, the future looks promising as Nektar continues to spend great amounts on drugs and their deliverance.

- **Partnerships and Collaborations**

A critical part of Nektar's business strategy is creating collaborative partnerships with major pharmaceutical companies; this allows them to offset the high costs of research and development by sharing their future revenues with collaborators if the drug passes all clinical stages and obtains approval from the governing agency. This business strategy enables continued operations and survival in such a competitive industry; by sharing revenues, the company as a whole develops much slower, but as a small cap firm, it is a suitable method to reduce the risk of running out of cash to fuel their costly research and development.

Looking at the development deal struck with AstraZeneca, this partnership alone gave them \$125 million up-front in order to continue research with the potential to obtain an addition \$1.5 billion in milestone payments. AstraZeneca has agreed to be responsible for the development, global manufacturing, and marketing of both Naloxegol and NKTR-119. This partnership and more importantly the decision on Naloxegol will be a key component of the financial health of Nektar for the upcoming years as it has had much money spent on R&D and can bring in enormous profits as it is a novel drug. As Nektar does not have the manufacturing or marketing factor of a large firm, they must continue looking for these key partners to bring their drugs to market.



Threats

- **Competitive Landscape**

As the quintessence of biotechnology/pharmaceutical companies is the discovery of drugs and delivery process, the rivalry among companies is very high as there are extremely large costs for research and development. It is crucial for firms to continually seek new treatments and begin the highly regulated clinical trial process for groundbreaking drugs, as revenue from these drugs is vital to the survival of each company; for this reason, each competitor rushes to file a New Drug Application with the governing agency, Food and Drug Administration (FDA) in the US and European Medicines Agency (EMA) in the European Union. Creating novel compounds that successfully treat a condition can be very lucrative, as patenting these drugs will usually lead to a monopoly in treatment of the condition for up to 12 years.²⁶

As profitable as these new medicines can be, the rejection of a drug by the central agency are massive setback for the company due to a huge financial loss from research costs. In order to embrace these obstructions, firms must have a large portfolio of drugs and technologies to strengthen the research and development pipeline. Companies that focus on creating new compounds and deliverance must also compete with the firms that concentrate on producing generic drugs that are not protected by patents; as these firms do not have large R&D spending, they are able to undercut the brand drugs to gain a profit while demolishing revenues for companies that originally developed the drugs.

- **Uncertainties in R&D Outcomes**

One of the biggest threats to continuing the current level of investment in research and development is the uncertainties in R&D outcomes. Drug development is a long and uncertain process with a high risk of failure at every stage of development even with the success in previously completed clinical trials; even with successfully completed clinical trials, the risk of clinical failure for any drug candidates is high due to factors such as inconclusive efficacy or safety. The failure of a drug candidate that is further into its clinical studies will

²⁶ www.healthreform.kff.org/timeline.aspx



create a greater adverse effect on Nektar's business, financial condition, and results of operations due to the exponential increase in costs for every sequential phase seen in Table 3.

- **New Government Regulations /Difficult Pricing due to PPACA**

Buyer's bargaining power is increasing with the implementation of the Patient Protection and Affordable Care Act. PPACA is aimed at increasing health insurance coverage rates in the US by reducing the overall costs of health care. With the elimination of co-payments and deductibles for select "essential" health care insurance benefits, firms are getting squeezed of profits.²⁷ Also, as PPACA are now requires insurances companies to cover all applicants at the same rates regardless of pre-existing conditions, this will lead the buyer, insurance companies in this case, to require cheaper pricing on drugs.²⁸ The threat of generic drugs has increased as the FDA is now authorized to approve generic drugs after only 12 years of exclusive use down from the previous, much longer 20 years; this will have a greatly negative impact on this industry as they have depended on the fact that they have exclusive use for 20 years in order to make up for the high costs of R&D.

Nektar's strengths and opportunities outweigh their weaknesses and threats, but the company is still very much risky because there is an enormous uncertainty of an FDA approval no matter how confident their executives and scientists are.

²⁷ "Essential Health Benefits" - www.healthcare.gov

²⁸ "ObamaCare Survives the Supreme Court" – www.theweek.com



STRATEGIC RECOMMENDATIONS

Gain a First Move Advantage by Focusing on Naloxegol

Nektar must concentrate on getting approval for Naloxegol by the FDA and EMA by conducting extensive research showing the drug program meets the regulatory laws. There are currently no oral drugs approved specifically for the treatment of opioid-induced constipation (OIC) or opioid bowel dysfunction (OBD). The only approved treatment for OIC is a subcutaneous treatment called methyl naltrexone bromide marketed by Salix Pharmaceuticals. As there are a number of companies developing very similar treatments to Naloxegol that are in various stages of clinical development, Nektar must gain a first mover advantage by first introducing a oral treatment for OIC and OBD²⁹; in doing so, Nektar will be able to obtain a large portion of the market and gain monopoly-like profit margins.

Naloxegol, which passed the final stage of clinical trials, is a novel drug and has many competitors striving to enter this sector for the treatment of opioid induced health problems. The \$14.8 billion global opioid market is the largest of the Global Chronic Pain Therapy Market with five main markets accounting for almost 80% of total unit volumes: US (49%), UK (14%), Germany (5%), Canada (5%), and France (5%). OIC is a significant unmet medical need with 69 million patients taking opioids for chronic pain and approximately 40-50% (28-35 million) of them who take opioids for an extended period of time develop constipation.³⁰ Nektar entered a global license agreement with AstraZeneca AB (AZ) to which AstraZeneca is responsible for all development, regulatory, and commercialization activities. With the proper guidance, Nektar is eligible for \$95 million in milestones upon US/EU acceptance of filings as well as up to \$140 million in launch and \$375 million in sales milestones. Other deals have included agreements for PEGASYS, a hepatitis C drug, and Macugen, an age-related macular degeneration drug with Roche and OSI Pharmaceuticals respectively.

By focusing on filing NDAs for the FDA and EMA, Nektar will receive crucial payments that will aid their large capital needs. Getting approval will allow them to get the first mover advantage into a market that is 28-35 million people in size. These milestone payments will help

²⁹ Nektar Therapeutics 10-K 2012

³⁰ IMS Health NPA MAT-2Q12



them make a push to become profitable.

Create a Brand for Themselves

Nektar must establish itself as a top quality biotechnology company. With approvals of key drugs such as Naloxegol and continuing to build their R&D pipeline, they can generate a greater demand for new partnerships for their novel drugs. By establishing a their drug platforms to be superior and bringing in large revenues, Nektar will build a brand for themselves as the top clinical-stage biopharmaceutical company. In an industry with such high internal rivalry, it is critical for workers to establish a positive reputation of being easy to work along and having constant, reliable clinical results such that major drug companies will continue their collaborative partnerships. Nektar must show the use of their advance proprietary technology base of PEGylation and Advance Polymer Conjugate technology in creating drugs exceeds any other drug implementing technology.

Gain Partnerships

Nektar is a highly capital-intensive company with its extensive R&D department; it is in their best interest to establish and maintain collaboration partnerships to succeed in this highly competitive market. These partnerships must be on attractive commercial terms, else the results of operations and financial condition will suffer greatly. Even with their inability to predict R&D outcomes, by creating these relations in the short-term, Nektar will obtain capital for further research and can grow at a steady pace until they are able to develop, test, and market without a partner. Another advantage of having collaborators with attractive agreements is being able to use the acquired capital to continue their trend of having a robust R&D pipeline.

Produce, Commercialize, and Market by Themselves in the Future

Nektar should continue implementing their current business strategy of procuring partnerships until they become profitable and hold excess cash after normal operations, at which point, they should look into obtaining their own facility where they can produce its own drugs. After analyzing the costs of creating and maintaining a pharmaceutical manufacturing plant, Bridges will be able to determine the appropriate timing of acquiring their own plant; in doing so, Nektar will inherently take on greater risk, but receiving all revenues, not just milestone payments, will exponentially grow their revenue correlating with the growth of their company and aid in creating a brand. By becoming a larger, brand-name company, the firm will have greater bargaining power



when dealing with suppliers as well as having a constant revenue stream instead of their large one-time payments for milestones that each drug achieves. This will combat the capital-intensive nature of this industry.

Create Products with Pricing Approvals by Government Authorities

With the governments attempt in making health care more affordable, the PPACA has set stricter regulations on the costs of a drug; this affects not only private insurance programs, but also public programs such as Medicare. Creating a product line that has pricing approval by government authorities and has availability of payment or reimbursement from third-party payers is important for the sales their approved products. If government and private insurance programs do not provide payment or reimbursement for our partnered products or proprietary products, those products will not be widely accepted, which would have a negative impact on their business, results of operations and financial condition. Nektar must provide drug candidates that are in line with the new PPACA pricing regulations to avoid rejection of the drug by any third-party payers.

Sell Off One of Their Drugs or Technology Platform

With the high cost of R&D, Bridges' recommends that Nektar be prepared to sell of one of the drugs in their pipeline in order for the continuance of the company through the lows of the uncertainty involved in clinical trials outcomes and NDA; this must be attempted before selling one of their proprietary platforms, which has proved to be very costly. In 2008, Nektar's revenues fell when it had to sell its pulmonary delivery assets, including approximately 140 of their dedicated pulmonary personal and operations to Novartis for \$115 million. The two firms had worked together on the development of Tobramycin inhalation powder (TIP), a potential treatment for cystic fibrosis.³¹ They were able to retain some drug programs involving their pulmonary delivery platform, including its inhaled vancomycin candidate; however, this, along with the lower demand for their manufacturing services, had a negative impact on their development plans. This recommendation of selling off one of their drug or technology platforms is a last resort if cash reserves and other cash equivalents run dangerously low.

³¹ Nektar Therapeutics 10-K 2012s