

# An Alternate Look

## at the Pharmaceutical World Revenues and Drug Affordability



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**W**orld Preview 2017, Outlook to 2022 [1] published by EvaluatePharma® is an interesting report. There are similar reports published every year. From a sales perspective these reports might be useful as to some, however, I have not seen a report that translates or equates sales numbers to number of patients served and/or affordability. Since developed countries (Haves) and developing countries (Have Nots) are two distinct customer bases, it would be useful to under-

stand drug expenditure spending per person, per day for each market. The resulting numbers could be used to understand and develop plans to improve global sales and affordability of drugs. These numbers might also tell us "whether projected sales from other forecasters can be achieved, where the sales could come from and what steps need to be taken to achieve the projected sales and make the product affordable."

Numbers from Exhibit 1 that are in Table 1 demonstrate what is required to meet sales projections.

**Worldwide Total Prescription Drug Sales (2008-2022)**

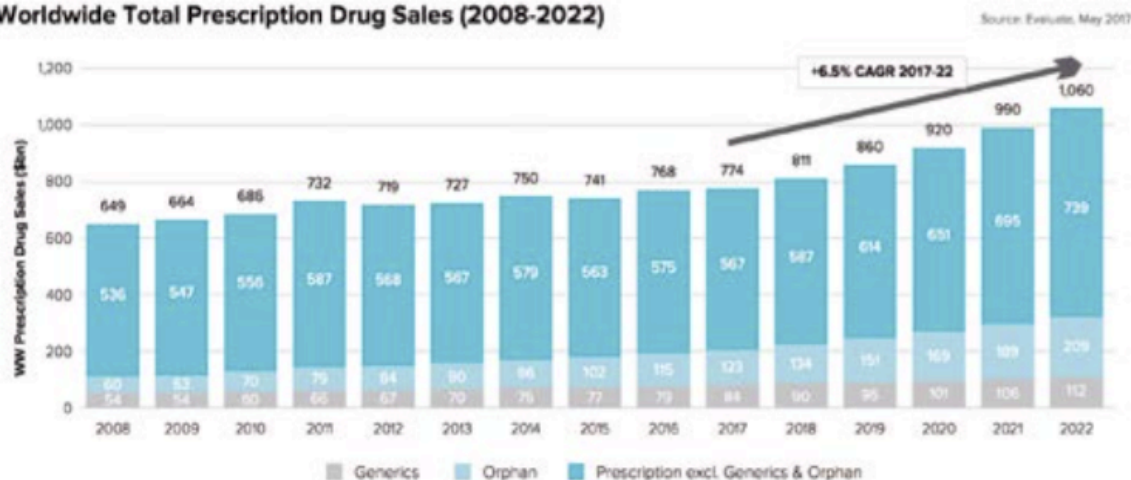


Exhibit 1: Page 8 [1]

Sales, \$ Billions	2017	2018	2019	2020	2021	2022
	Differential Sales increase over the previous year, \$ Billions					
Generic	84	6	5	6	5	6
Orphan, (% of Total Sales)	123 (15.9)	11 (16.5)	17 (17.6)	18 (18.4)	20 (19.1)	20 (19.7)
Prescription Excl. Generic & Orphan	567	20	27	37	44	44
Total	774	811	860	920	990	1060
Differential \$ gain over previous year, Billions		37	49	60	70	70

Table 1: Sales and Differential Sales

The numbers in Table 1 seem realistic and obtainable, however the projected sales increase for each year is equivalent [2] to the revenue of one or two of the top FIVE pharmaceutical companies for the next five years. Therefore, achieving these numbers is easier said than done. An earlier alternate study reviewing drug prices and number of patients might be of interest [3].

Table 2 has been created using the sales forecast from Table 1. The population of the developed and the developing countries and average sale per person per day in the developing countries [4] are used to determine the sales for the developed countries. Average sales per day per person for the developing countries including the rest of the world might be considered low, but using the available data [5,6] and extrapolating it, it is the best number I could derive. I am comfortable with the developed

numbers. In my travels and personal experiences, I have seen that prices for the prescription and generics in developing countries are significantly lower, than the prices for the same prescriptions in developed countries. However, even with low prices, people in developing countries have to decide between food for the family and drugs for the ill family member/s [7], as a result of low incomes.

Based on the sales increase from 2008 to 2016 [Exhibit 1], one can speculate that the projected 2022 sales will mostly come from the developed countries, rather than the developing countries. Orphan drugs (less than 200,000 patients per disease) are going to be an ever-increasing source of revenue and as a result, Brand pharma have shifted their focus from drugs for the masses, to orphan drugs. It is well-known that orphan drugs increase revenue dramatically as they are very highly priced

and also highly profitable. New drugs are being introduced continuously, but most are only marginally [8] better than the drugs already on the market and are equally expensive. As a result, they are unaffordable to many and frowned upon even by physicians and healthcare systems. For example, PCSK9 is a class of drugs for cholesterol that will have a very limited market.

In recent years there has been a focus on increasing the prices of drugs rather than developing affordable drugs. A recent observation [9] ("Rather than compete by lowering net prices, the drug companies compete by raising list prices" says Berman, the managing partner of Hagens Berman Sobol Shapiro LLP) makes an interesting point about how pharmaceutical companies raise revenue.

Affordability in the developing countries is critical for sales. Merck [10]

Year ->	2017	2018	2019	2020	2021	2022
Global Sales, \$ Billions	774	811	860	920	990	1,060
Global population, Billions [5]	7.5	7.6	7.7	7.7	7.8	7.9
Increase 1% per yr.	6	6.08	6.16	6.16	6.24	6.32
Population outside Developed Countries, Billions (~80% of total)	175.2	177.5	179.9	179.9	182.2	184.5
Total Drug spending in Developing Countries \$ Billions, (basis \$0.08 [5,6] per person per day)	1.5	1.52	1.54	1.54	1.56	1.58
Developed Countries population, Billions, Increase 1% per yr.	598.8	633.5	680.1	740.1	807.8	875.5
Total Drug Sales in Developed Countries, \$ Billions	1.09	1.14	1.21	1.32	1.42	1.52
Total Drug \$ spending Developed Countries per person per day	3.42	3.57	3.78	4.11	4.43	4.74

Numbers are rounded

Table 2: Global Sales for the Developed, Developing countries and Sales Per Capita per person



Year	Sales Increase, Billions					
	2017	2018	2019	2020	2021	2022
Sales Increase from One cent per person per day across the world, \$ Billions	27.4	27.7	28.1	28.1	28.5	28.8
\$ Needed to meet revenue, Billions	6	37	49	60	70	70
Shortfall, \$ Billions	(-21.4)	6.3	20.9	31.9	41.5	41.2

Table 3: Value of One-Cent Price Increase vs. Global Sales Increases Needed per Year

in 2008 had to significantly lower the price of Januvia in India, a country with the highest population of individuals with diabetes. Affordability forced patients to stay with metformin hydrochloride or other drugs over Januvia. HIV drugs were unaffordable to many in Asia and Africa till Cipla Inc. [11] intervened and Gates and Clinton Foundations supported the move, although they remain expensive in the United States. If some of the infectious diseases were not present in developed countries, it is possible that companies may not have developed the necessary drugs.

HCV drug Sovaldi, sold in the US at \$84,000, is sold in India [12] and other countries for less than 200 times the US sale price by Gilead, through its arrangements with the local pharmaceutical companies. Compulsory licensing [13] is part of the WTO agreement and has been used to lower drug prices in the developing countries, which is not ideal for branded drug companies. However, affordability is critical and branded companies occasionally forget that some of their customers cannot even afford food at times [7]. Another important fact that brand companies forget is that they have more patients in need of the drug in developing countries rather than in the developed countries. Economies of scale can lower costs and improve profits.

Even with an excellent mutually subsidized healthcare system of the United States, it is well known that many patients do not take their drugs as prescribed [14,15,16].

Table 2 shows that the sales in the developed countries are going to stay at about four times the sales of the developing countries. This is very telling especially when the population of the developing countries is about four times of the developed countries. This lopsided arithmetic suggests that pharma companies have tremendous opportunities to increase their sales if drugs can become affordable.

## POTENTIAL WAYS TO INCREASE SALES AND IMPROVE AFFORDABILITY

With the current push to make drugs affordable in the United States and in other developed countries, pharmaceutical companies will be challenged to increase their revenue. Besides revenue increase through the sales of high-priced orphan drugs, affordability of the drugs to 80% of the population outside the developed countries is critical to driving sales. If this population cannot afford the necessary drugs, it is going to be a challenge to achieve the projected sales.

Developed countries have the highest usage of drugs. Pharmaceutical sales in the United States are nearly half [17] of the developed country sales. Marginally better drugs are taking up significant financial and manpower resources and have less than expected return. For sales to increase new drugs have to be substantially better than the current drugs on the market, however affordability will always play a significant role.

There are few ways sales can be improved and the options are discussed below, however these will not suit the business model of each company. Effort has to come from the companies rather than outside.

### 1) INCREASE PRICES

This could be considered the easiest way, but it will have the highest negative publicity along with lawsuits [9]. Table 3 shows the net effect of such increase. Sales shortfall from the projected numbers will still be there even when the average price is increased by one cent per person per day.

### 2) LOWER COSTS [18]

There are many different areas where costs can be lowered. They will come from improvements in regulatory processes and manufacturing technologies

and processes. Money saved will more than offset the investment costs necessary for such projects. Economies of scale can also significantly reduce costs and improve product quality. Lower prices could increase the patient base resulting in higher sales revenues.

#### ◀ Lower Regulatory Costs:

FDA's application, review and approval process of NDA and ANDA is based on analysis and re-analysis of the application, and this process is similar to a manufacturing process. FDA and regulators have suggested that companies should incorporate QbD (quality by design) practices in their manufacturing processes. May be the regulators should show the industry how incorporating QbD practices in their own workings will improve application approval quality leading to reduced approval time and associated costs. Recent efforts [19,20,21] have been made to shorten the filing and approval time. Continuous improvement effort is needed. Industry should not be told to improve their practices, the effort should come from within (quality by desire) as they reduce drug approval time.

#### ◀ Lower Manufacturing Costs:

There are many excellent ways to lower manufacturing costs. Fundamentals of chemical engineering and chemistry that are judiciously practiced in the chemical and petrochemical industries have to be applied. Cross-fertilization is necessary. Unit processes and unit operations can be significantly improved. We have to exploit physical and chemical behavior [22, 23] of the chemicals along with existing commercially available equipment can be creatively exploited to simplify reactive and formulation processes.

A simple example is to ensure that no more than two solvents, one being water, are used in the process. Multiple solvents suggests that the manufacturing process has not been optimized and

is similar to the laboratory synthesis, that is generally expensive due to poor conversion yields and methodology. Exploiting melting point differences, mutual solubility and density differences can simplify processes.

Most of the lab processes are dependent on measuring conversion and product quality during the reactive and formulation processes. Command of processes simplifies manufacturing and lowers costs while producing quality products from the start. As much as 25% savings [24] have been documented.

There are other ways manufacturing costs can be lowered which are process and product volume dependent. An important issue, asset utilization, is overlooked. In the manufacture of active ingredients and formulations, asset utilization is generally less than 50% [25]. Even though this reference is old, not much has changed when it comes to pharma's asset utilization. Poor asset utilization raises product costs and is an opportunity to improve profits.

#### ◀ Supply Chain:

Inventory turns better than pharma's current 1-2 turns make a big difference on business, a well-known fact. They force better control of raw materials, work in process and finished goods inventories. Cash flow improvement has big financial impact on costs. A lot of the suggestions can be achieved if we have excellent economic processes.

#### ◀ Process Waste:

Better processes have higher yield and thus lower costs. Command of processes produces quality products from the start rather than produce products through repeated analysis (aggravation). A better five step process with 95% yield at every step would have about 77% yield, compared to similar process having about 14% yield if each step had an initial yield of 67%. Higher yields reduce product cost and reduce environmental remediation burden. There is another benefit of high yield. We have to remember that most of the

drugs, even though they are fine/specialty chemicals, are highly toxic and they kill disease-causing bacteria to cure diseases. Thus, processes with low conversion yield and waste that is not properly disposed can have significant impact on aquatic, land, and human life.

Making drugs affordable is the best long-term way to improve the total sales in the developing countries. Because of the income differences between developed and developing countries, the differences in drug process will remain for the foreseeable future. Economies of scale and better manufacturing technologies [26] can make drugs affordable and increase sales. However, to achieve all this will require business model review and change. It is not an easy task for an industry that has not aggressively embraced change and innovation. Their focus has always been on new drug development and marketing, drug affordability is an unknown area. ■

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