CUBICASSET MANAGEMENT, LLC

2015 2nd Quarter Stock Market Commentary

BIGGER THAN ELVIS

"You may not be able to read a doctor's handwriting and prescription,
but you'll notice his bills are neatly typewritten."
- Earl Wilson

In 1946 the University of Pennsylvania's Moore School of Electrical Engineering introduced ENIAC (Electronic Numerical Integrator and Computer) the world's first general purpose computer. Construction was financed by the United States Army Ordnance Corps, who used it to calculate artillery firing tables. Each bit of information was stored on a single thumb sized vacuum tube, and there were 17,500 tubes used. The machine itself was 100 feet long, eight feet high and three feet deep, and required another 10,800 square feet for the air conditioning equipment needed to keep it cool because of the heat generated by all of the vacuum tubes. ENIAC was capable of performing 5,000 computations per second.

A decade later a new generation of computers was built which replaced the vacuum tubes with newly invented transistors.

The next big leap forward was in 1964, when transistors were replaced with integrated circuits. This innovation dramatically increased the speed and efficiency of computers, and allowed for the running of multiple applications at the same time. These refrigerator-sized third generation mainframes were capable of performing on the order of 200,000 instructions per second, roughly 40 times the speed of first generation machines, had memory of up to two megabytes, and cost several hundred thousand dollars.

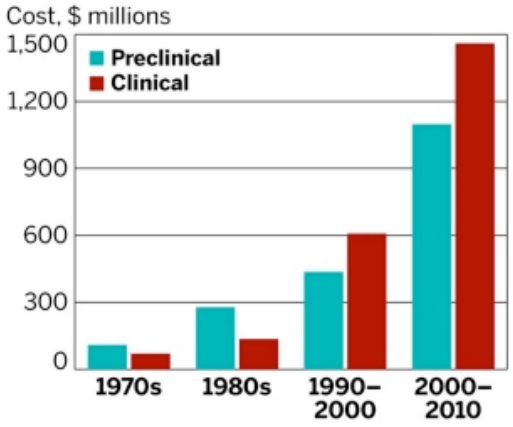
Today's smart phones, which cost only a few hundred dollars, are capable of executing over 28 billion instructions per second with 128 gigabytes of memory, and yet are small enough to fit in a pocket.

This exponential reduction in size and increase in speed gave rise to a statement that has since been dubbed Moore's Law. In 1965 Gordon Moore, co-founder of Intel, postulated that the number of transistors in an integrated circuit could be expected to double every year, a figure he later revised to every two years. While not really a natural law, but rather an observation, Moore's Law has reasonably described the improvement in performance and reduction in size and price of today's electronic devices.

The pharmaceutical industry is another area in which research and development has led to dramatic scientific advances. Unlike the electronics industry, though, the cost of breakthroughs has been soaring, driving the cost of drugs up sharply. Consider, as an example, Gilead Pharmaceutical's blockbuster drug Sovaldi to treat Hepatitis C. Hepatitis is a disease characterized by inflammation of the liver. While it can be caused by drugs or other toxins, or occasionally by bacteria or fungus, it is primarily a viral infection. The virus that causes Hepatitis B was first identified in 1963, followed by the identification of the virus responsible for Hepatitis A ten years later. All other forms of the disease were simply called non-A, non-B. In 1989 scientists working for the Centers for Disease Control isolated the virus responsible for what is now called Hepatitis C, which represents roughly 95% of the non-A, non-B cases. Up until recently, the standard of care for the treatment of the disease was interferon (with or without another antiviral ribavirin). This was successful roughly 20-60% of the time, with the wide variation depending upon the specific genotype of the virus. Interferon is a nasty drug, which can cause depression and mood changes, insomnia, depressed white cells and platelets, nausea and muscle aches, to name only a few of the side effects. For the majority of people the treatment was unsuccessful, often leading to liver failure. Unfortunately, there is a chronic shortage of liver donors, so that many die on the transplant waiting list.

By contrast, Sovaldi, approved in 2013, results in a complete cure for 90-96% of patients. But there is a catch - the twelve week treatment costs a staggering $84,000, based upon the wholesale price of the drug. This high cost drug has single-handedly ignited a fierce debate about the appropriate level of specialty pharmaceuticals pricing in the U.S. Why are drug prices so high?

Consider the chart shown at the right prepared by the Tufts Center for the Study of Drug Development. In the 1970s, it cost roughly $150 million to bring a new drug to market. In the 1980s that figure had risen to nearly $450 million. Currently, that figure has risen to approximately $2.6 billion.



In a terrific article in Nature Reviews Drug Discovery entitled *Diagnosing the Decline in Pharmaceutical R&D Efficiency*, authors Jack W. Scannell, Alex Blanckley, Helen Boldon & Brian Warrington showed that the number of new drugs developed per billion dollars of research and development spending has been dropping exponentially for 60 years. They dubbed this Eroom's Law. The word EROOM is simply MOORE spelled backwards, and this was a clever way to indicate that this decline in efficiency was the inverse of the increases experienced in electronics.

The authors identified four factors whose combined drag has outweighed scientific, technical and managerial advances. The first of these they dub the "Better than the Beatles" problem, but which I prefer to call Bigger than Elvis. Imagine how difficult it would be to produce a hit record if it could only be marketed if it was better than any record ever put out by the King of Rock & Roll. That is analogous to the situation in bringing a new drug to market. Effective treatments are hard to supplant. Aspirin (or acetylsalicilic acid) has been marketed since 1899 (although the Egyptians were known to use salycilic tea in 400 BC to reduce fevers) and continues to sell well. Lipitor, now available in generic form, is quite effective at reducing LDL cholesterol, discouraging other companies from trying to develop alternatives.

Because of the fact that most of the diseases that affect large numbers of people have effective treatments, drug companies have been producing more "orphan" drugs, defined to be drugs that treat diseases which affect no more than 200,000 individuals, where no effective therapies exist. Orphan drug designation allows companies to have a longer period of marketing exclusivity (7 years) and tax credits for clinical research. Last year over 40% of new drug approvals were for orphan drugs.

The lack of competition provides the ability to price orphan drugs very high. In 2012 the FDA granted approval to orphan drug Kalydeco produced by Vertex Pharmaceuticals, which is used to treat a rare form of cystic fibrosis affecting only a few thousand people. This drug is currently priced at $306,000 per year. Less than two months ago Alexion Pharmaceuticals announced the acquisition of Lexington, Massachusetts based Synageva BioPharma Corp. for $8.4 billion, a staggering price for a company which has never had a single penny of revenue because it has no products for sale. It does, however, have a new drug in late stage clinical trials to treat Lysosomal Acid Lipase Deficiency, an extremely rare disorder which affects less than 3,000 people in the world. Imagine how high the price will have to be to provide a decent return on that investment.

The second factor the authors identified as causing high prices is the increased caution on the part of regulators who approve new drugs. In the late 1950s and early 1960s the public was horrified when a drug used to treat morning sickness in pregnant women, thalidomide, turned out to cause children to be born with malformed or missing limbs. More recently, a class of anti-inflammatory drugs called Cox-2 inhibitors turned out to be associated with an increased number of heart attacks and strokes. This led to Merck's Vioxx being forced off the market in 2004, and has prompted the FDA to demand considerably more data before granting the right to market a new compound.

The third factor is that drug companies have not been historically good at allocating capital, and tend to waste a lot of what they spend. In the advertising business there is an old saying attributed to John Wanamaker that "Half the money I spend on advertising is wasted; the trouble is I don't know which half." Drug discovery and development is similar, in that there is a great deal of serendipity involved, and it is nearly impossible to know in advance what research will produce results.

Lastly, the authors point out that modern high-volume screening techniques make it possible to test very large numbers of molecules through sheer brute force, an expensive approach.

There is another factor not identified by the authors which I call the Leapfrog Effect. In order to understand it, consider an analog in the world of real estate. In 1980 the average Boston condominium sold for under $100,000. An investor who purchased a unit and rented it out for income would have gotten roughly $500/month at the time. But the cost of a condominium in Boston has increased sharply over the years. The typical apartment now costs $1,000,000. Rents have risen, too, although not as fast, so that the average rent in today Boston is $2,200. Undoubtedly, the rent for the original apartment is in line with the higher figure, even if it is still owned by the original buyer. As the cost of new units has risen, rents have leapfrogged higher, whether or not the unit has changed hands. Every owner mentally marks-to-market his/her property and charges a rent which provides a return on that higher valuation.

The same thing occurs in pricing drugs. As noted earlier, it cost $400 million to bring a new drug to market in 1980, compared to $2.6 billion today. Many companies raise the price of their drugs to provide an adequate return on that higher figure, whether or not that represents their historical cost. If they do not, someone else will do it for them through acquisition. The poster child for this is the Canadian company Valeant Pharmaceuticals. On February 10 of this year they acquired the rights to two drugs, vasodilator Nitropress and Isuprel, for bradycardia. On that same date they raised the price of the drugs by 525% and 212%, respectively. But Valeant is hardly alone. Horizon Pharma bought the rights to Vimovo pain tablets from AstraZeneca in late 2013. On January 1, 2014 they raised the price by 597%. Mallinckrodt acquired Cadence Pharmaceuticals and raised the price of its pain killer Ofirmev by 250% three months later.

Unfortunately, the forces driving higher drug development costs, followed by higher prices for patients, show no sign of abating. Smaller pharmaceutical companies with narrowly focused research efforts continue to find many promising new drug candidates, but only 20% of them will advance from Phase 1 trials to market approval. The staggering cost of the process forces many early stage companies to sell out to deep-pocketed big pharma. Similarly, the largest drug companies need to keep refreshing their new drug pipeline, as well as to leverage their marketing efforts across a larger sales base. At least in drug development, size matters. This year Johnson & Johnson acquired Swiss biotech firm AC Immune, Dublin based Shire bought NPS Pharmaceuticals, Actavis completed the acquisition of Allergan, the Canadian company Valeant swallowed up Salix, and Pfizer purchased Hospira, to name but a few deals. For investors, this means either buying a portfolio of smaller biotech companies with promising drugs in early stage trials in the hope that some of them will be purchased for a huge premium, or buying big pharma, who have the marketing, distribution and capital to exploit these products worldwide. Either way, today's high multiples seem likely to be higher tomorrow.