Pharma Business avalanche Modeling through the strategy game of GO

By Shavit Fragman



Small Avalanche joseki

Real Avalanche

Large Avalanche joseki

Summary:

GO is the oldest strategy board game in the world.

We discuss analogy between GO and business.

Analyzing business strategy and positions through the GO prism can provide new, deeper insights to senior level management.

\$100 billion are about to evaporate from big pharma revenues in the coming years due to patent expirations and generic substitute arrival.

The avalanche joseki is used as a metaphor to understand the near future that global pharma business face. It also reflects high risk strategy.

In addition, some corporations basic strategy is viewed and interpreted via this tool. We strongly encourage GO skills to senior management.

Introduction:

In the article we will present and discuss an interpretation of the avalanche phenomena occurring in the pharma industry through the strategy game of GO.

We find similarity between GO and business. We present a modeling of corporate strategy, choice of direction and decision making through GO.

One of the ultimate risks when climbing the Everest and the highest mountains is an avalanche (on top of so many other risks). Experienced climbers know how critical every step they make and how they anchor themselves. Many fail to reach the top, or survive the way back. One small mistake may lead to a massive life threatening fall.

High skill is a must for high mountain climbers. Similarly in the game of GO.

GO is a game of pure skill, where all your focus and attention must be at their prime throughout the game.

We use the "Avalanche" as a metaphor to the expected decline of revenues and profits in the pharma industry induced by patent expiry in the coming years.

Coming from the pharma and healthcare arena my examples will be from this market.

Background on the strategy game of GO

For those who are less experienced with the game it is easier to grasp it as a "market share" game. In the beginning my lectures, it is presented this way, but that is undermining the game.

Go is an ancient strategy board game, invented in China about 4,000 years ago. Some claim that Emperor Yao invented it for his son to gain management and thinking skills. The game arrived to Japan by a Buddhist monk or the Japanese ambassador in China. Soon after it became popular and turned into Japan's national game. In China Wei'Chi (Go) is considered one of the 4 accomplishments. In Japan it is one of the 4 arts any noble man or woman should master. Go is both an Art and a Martial art. Its popularity has now exceeded 60 million players worldwide.

Go combines simple elements of wood, stones (Black & White, Yin-Yang), circle and lines, that create an amazing pattern on the goban (Go board) and infinite game sequences, which embrace creativity, aesthetics, thinking and reasoning to their highest level.

The game is played on a 19x19 grid. The goal of the game is to surround territory. Stones are placed on the intersections. In this game, each player places a biconvex stone on an intersection. Each player builds his own territory, by surrounding vacant intersection. In the course of the game the players must defend their prospected territory and it is possible to invade as well as capture opponent stones.

Go is considered a reflection of life and there are many eastern philosophies such as Buddhism and Zen are immersed in it. Self-control and punishment for greed are taught.

GO involves elements such as memory, cognition, decision-making and problem-solving.

Critical thinking is a complicated process that involves a number of skills such as gathering information, evaluating data and making logical conclusions and hypotheses.

Reasoning is a meta-skill because it involves analyses and a decision-making process for real-world situations. All of these skills are used and exercised in go, making it the ultimate tool to acquire these skills and the pursuit for excellence.

Analysis skills, global view combined with appreciation of situations are developed by players. Strategic thinking and tactical maneuvering are perfected.

Go is taught in several universities as part of the curriculum of MBA programs.

In Korea Baduk (Go) is studied at Myongji University.

Go is an amazing tool for developing executive, managerial and leadership skills. Throughout the game decisions must be made. Tradeoffs are evaluated, decisions are made and priorities are set. Strategies and tactics are decided and executed.

Let us examine this rolling dice: made this way.

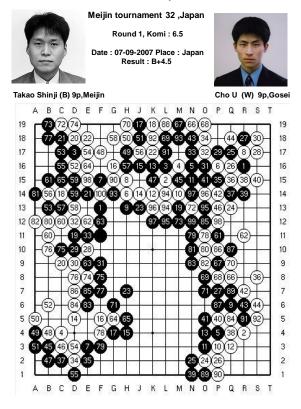
When evaluating a position or analysed. Similarly in Go -

Corporate decision, as in Go, are not

situation in business, it is throughly positional judgement is carried throughout

the game, tardeoffs are mapped and risk assessemnt performed naturally.

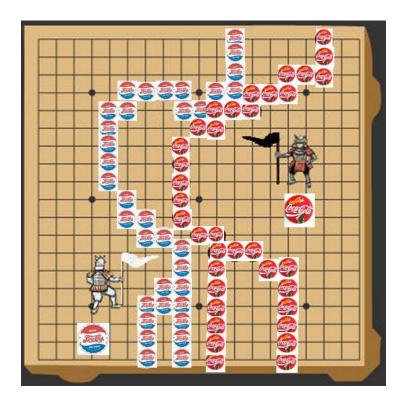
Look at the following game record (kifu) and you can easily see how different areas of the board are surrounded by white stones, while other areas are surrounded by black stones.



The business equivalent

What happens when we switch the white and black stones with Coca Cola and Pepsi cups?

Did we say "market share"?





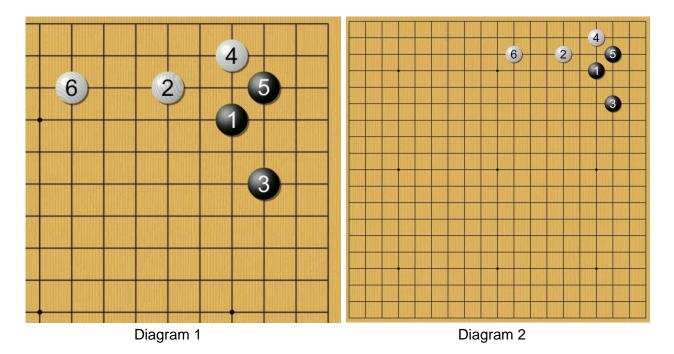
Vs



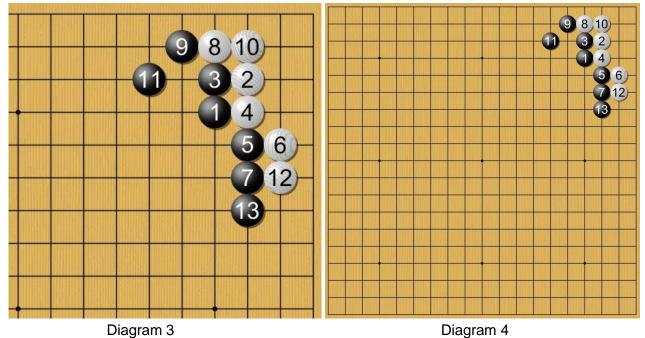
In the game of GO a "Joseki" is a local set of sequential moves that leads, when played accurately and skillfully, to equal result to both players.

This is what we call a "Win – Win" situation in business. If you do not play skillfully you end up with a loss.

Here is a demonstration of 2 very basic joseki that demonstrate the "Win-Win" result:



In diagram 1 we can see how both players divide the corner area with the sequence to move 6. Both players end up having same equivalent gain from their position. Black's territory seems a bit smaller than white's, but he has his next move in "sente" (advantage) and has the priority to take a new strategic position.

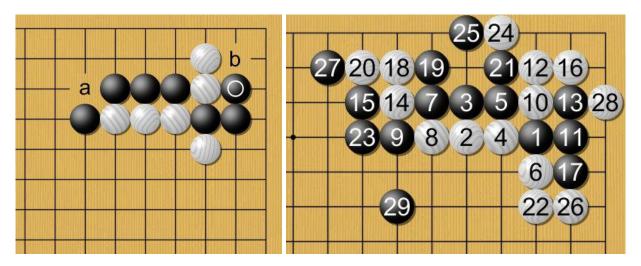


Diagrams 3 and 4 demonstrate another common joseki, which leads to black getting outside "influence" towards the center, while black gains some corner territory.

The Japanese term Nadare (mireobuchigi in Korean and xuebeng in Chinese) means avalanche. This sequence may lead to very complex variations and careful maneuver concentration and skill is a must. The name was coined during the Showa period 1926-84. Playing Nadare joseki requires top skill and artful finesse to overcome the chasm waiting for the less skilled player. "Win Win" or "Abyss".

There are 2 avalanche joseki: the small and large avalanche/ Nadare. However, these 2 josekis lead to very complex situations and variations. One mistake and an avalanche occur, leading to a painful loss on the board.

Here is a taste of the avalanche joseki:



Black 13 was invented by Wu Qingyuan = Go Seigen, played first on February 2, 1957 against Takagawa. The move was considered revolutionary. This innovative move has transformed the large avalanche joseki, Although the variation of Go Seigen it isn't up to date anymore in the new millenium, there are other continuations who are still considered joseki. White continues with 'a'. White 'b' is not recommended.

Therefore, playing the avalanche joseki is like walking on the edge of a slippery cliff.

The question to the CEO should be: What are you aiming at / for, when you play nadare?



Or as Donna Summer phrased it: "Do you know, where you're going to?

Let's have a look at some of the big players in the pharmaceuticals business and see how we can understand their position using the GO thinking.

We will look at the pharma market trends for the rest of the decade and will elaborate further over some of them. Then we will use this approach to appreciate some of the smaller players.

Current Pharma industry trends:

The pharmaceutical industry, is faced with threats to its future revenues.

Different companies adopted different strategies. Some of them may be related with the avalanche joseki.

It is interesting to note that Morgan Stanley recently used "An Avalanche of Risk?" while downgrading an entire group of multinational pharmaceutical companies based in Europe. "The operating environment for pharma is worsening rapidly."

One of the objectives during the game of GO is to try and achieve maximal efficiency -Return on Investment, from every move.

The pharma industry extended research and development spending and has nearly doubled to \$45 billion a year over the last decade. However, the Food and Drug Administration has approved fewer and fewer new drugs. Pfizer and Eli Lilly had major setbacks last year in once-promising Alzheimer's drug experiments. Merck stopped testing its top acquisition from its merger with Schering Plough, a blood thinner that caused dangerous amounts of bleeding.

The industry's best-selling drugs will lose patent protection in 2011-12. An estimated \$50 billion of sales will diminish thereafter. Another \$50 billion is expected to vanish by 2015. Drugs in development may not offset the hit to sales. The "patent cliff" weighs on sector valuations—currently near historic lows—but is particularly acute for "pure play" pharmaceutical groups Eli Lilly, Bristol-Myers Squibb and AstraZeneca.

More diversified groups currently enjoy higher valuations, adding to the pressure to do deals. Targets are likely to include branded emerging-market generic-drug makers, diagnostics firms that offer proprietary drug-testing expertise and consumer-health firms that avoid the risks of government health-care cuts. However, valuations have already risen in anticipation, putting them out of reach of pharmaceutical firms that lack synergies.

Several of the drug giants have bought competitors with newer products to refill their own portfolio and sales gaps, essentially paying cash for future revenue as their own research was flagging. In the last two years, Pfizer paid \$68 billion for Wyeth, Merck paid \$41 billion for Schering-Plough, Roche paid \$46 billion for Genentech, and Sanofi-Aventis paid \$20 billion for Genzyme.

At the end of November 2011, Pfizer is about to lose a \$10-billion-a-year revenue stream when the patent on its blockbuster cholesterol drug Lipitor expires and cheaper generics begin to cut into the company's huge sales.

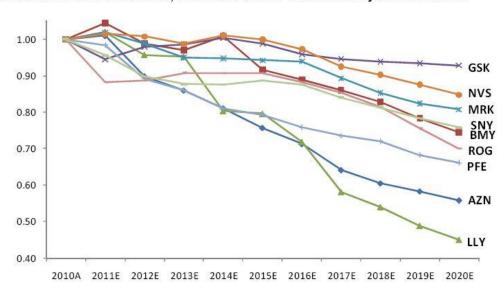
We will use the GO Japanese term "Moyo" – Framework to describe the infiltration of

generics. While patent is valid, the owner has full access to its luxurious benefits (high price, market share). Once patent is off, generics join the market, erode and nibble its value, profits and market share.

On top, the implementation of the US Healthcare reform and an intensifying of European pricing actions under the banner of "austerity", put extra pressure on the market.2010 yielded poorly in the number of product launches as well as R&D productivity.

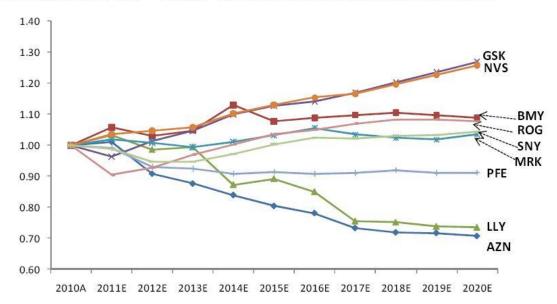
Let's look at some charts analyzing the pharma market and company expected performance.

Here is Anderson's chart showing percentage revenue declines for companies' existing drug portfolios:



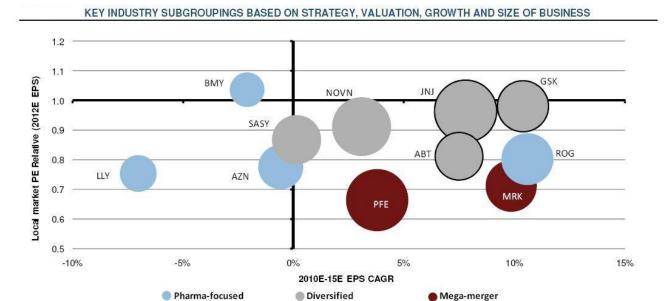
"Base" Pharmaceutical Revenues to 2020, Normalized to 2010* - A Remarkably Variable Outlook

Here is Anderson's revenue scenario counting current products, including expected launch of products in the pipeline, and non-drug revenues:



Total Company Revenues ("Base" + Pipeline + Non-Pharma Divisions) to 2020, Normalized to 2010*

Here is another view and analysis by Jefferies Iternational:



Source: Jefferies research

Patent Expiration of 10 Top Selling Drugs Each Year

2010		2011		2012		2013	
Product	2009 Sales (\$MM)	Product	2009 Sales (\$MM)	Product	2009 Sales (\$MM)	Product	2009 Sales (\$MM)
Aricept	3,991	Lipitor	12,535	Plavix	9,801	Cymbalta	4,660
Cozaar	3,561	Advair	7,794	Enbrel	6,575	АсірНех	2,728
Effexor XR	3,182	Zyprexa	4,916	Diovan	6,013	Humalog	1,959
Taxolere	3,034	Levaquin	2,648	Seroquel	5,126	Zometa	1,469
Protonix	2,052	Xalatan	1,737	Singulair	4,660	Niaspan*	853
Flomax	1,970	Concerta*	1,326	Lexapro	3,263	Lovaza	705
Arimidex	1,921	Femara	1,292	Avapro	3,088	Xopenex^	357
Gemzar	1,363	Xeloda	1,160	Actos	2,532	Zomig^	166
NovoSeven	1,320	Avelox	1,020	Viagra	1,892	Advicor*	80
Coreg^	253	Caduet	548	Avandia	/24	Fuzeon^	26
Total	\$22,647	Total	\$34,976	Total	\$43,674	Total	\$13,003

*Year of first available generic

^US Sales only

Source: Ken Kaitin, Tufts University, SCB's Pharma. R&D Productivity Conference, May 5, 2011

AstraZeneca

The company is about to lose patent of its key drug Seroquel (USA-2012). The company has other patents expiring in the period 2012-15. Revenues are expected to decline from 33B\$ to 23B\$. However, Seroquel happens to be a highly profitable drug, accounting for almost half the company's pretax profits.

Unlike its rivals in the industry, who expand via acquisitions and diversification, the pharma giant is determined to find new drugs in its own research and development labs. AstraZeneca is sticking to one business: developing pharmaceuticals innovative enough to command premium prices. AstraZeneca is alone with this strategy relying on self-drug discovery. On top of that, statistics indicate that the company has been one of the worst performers among big drug makers in obtaining approval for new medicines in the U.S. or the European Union in the past three years. Four of its potential blockbuster cardiovascular or diabetes drugs that failed in late-stage trials from 2006 to 2008. Industry rivals claim that they are destroying value by investing in research and development. In order to increase chances, improve productivity and limit downfalls AZ has narrowed the scope of research to focus on more promising areas such as diabetes and cancer, and has shut some sites to save \$1 billion annually by 2014.

The semi good news were when AstraZeneca got permission in December to sell Brilinta, the company's most important experimental product, in the EU. The clot-preventing drug proved more effective in studies than Sanofi-Aventis' and Bristol-Myers Squibb's Plavix, which had nearly \$10 billion in sales in 2009. The FDA however did not grant license and asked for more clinical data.

"When you have an enormous patent cliff, poor record of returns in R&D, and no diversification, what do you do?"

Does it sound like the Avalanche/ Nadare Joseki? Do you hear the cliff collapse roar?

In summary: While other big drug makers are diversifying beyond pharmaceuticals, AstraZeneca is sticking with a risky in-house drug development strategy. AstraZeneca 's CEO David Brennan, must play the complex nadare joseki skillfully.

Let's hope he will not face the guillotine...

Eli Lilly

Eli Lilly had ~\$23 billion sales from its drug portfolio in 2010.

The company's sales portfolio is comprised of Neurology/ Psychiatry (45% of 2010 Sales), Endocrinology (28% of 2010 Sales), Oncology (16% of 2010 Sales), and Cardiovascular (10% of 2010 Sales) drugs.

As of April 2011, Eli Lilly's most profitable drug, Zyprexa, lost its patent protection, exposing it to generic competition. Zyprexa sales reached \$5 billion and constituted 24% of Eli Lilly's total sales for 2010. The loss of patent exclusivity will cut into its market share and cause lower pricing for the drug. Some market experts estimate that the company's overall revenues from its drug will be cut in half.

Developing a new drug is a time-consuming and high cost endeavor. The entire process of developing a new drug and bringing it to the market takes up to 10-15 years. On average it costs \$800 million. The majority of Eli Lilly's pipeline is comprised of potential cancer treating compounds. In addition, there are also candidates for the treatment of diabetes, alzheimer's disease, depression, and schizophrenia in late-stage clinical trials. These potential drugs will need to go through the evaluation of the major regulatory bodies.

Safety, efficacy and quality will need to be fully demonstrated. Once approved, they will need to survive the competition.

So the company is now facing a huge chasm to cross.

The strategy of relying on one mega drug (Zyprexa) that delivers 40% of revenues is dangerous. The good news are that the rest of their patent portfolio is young. Again, we sense the melting of snow under the company's path and the avalanche danger.

<u>Pfizer</u>

Pfizer is a far more diversified company. However, it aims to quickly expand in fast-growing emerging markets—an area it is counting on to help offset the loss of its top-selling product.

Sales in emerging markets account for about 18% of Pfizer's revenue, and drug sales in the countries grew at a rate of 40% so far this year not including foreign exchange, according to the company. Emerging markets represent "a major growth opportunity" for Pfizer. However, these markets are learning very fast how to contain the cost of medicines – How does that sound in GO terms as "reducing a moyo or opponents territory?"

Pfizer needs to learn how to offset the loss of a fifth of its yearly revenue, more than \$11 billion, once cholesterol fighter Lipitor starts facing generic competition next year - 2012.

Companies who are "one product" companies seem to follow one of the avalanche paths.

Their key threat is when their blockbuster drug will go off patent and generics with "invade" their "moyo" – framework.

<u>Actelion</u>

Actelion has one star drug—Tracleer, for the treatment of pulmonary arterial hypertension, or PAH. In their portfolio, at the moment are low volume products and a high-risk R&D pipeline. Many consider this company to be on the table for a merger, but it is difficult to find attractive synergies that will allow a premium return on such investment. Tracleer has five to seven years' of blockbuster sales before its patents expire first in the U.S. and then in Europe. This means that the "guaranteed" income stream may be stopped. The key unknown factor is Actelion's pipeline. This year's failure of its hemorrhage project clazosentan, centers on two Phase III projects: almorexant, partnered with GSK for insomnia, and macitentan for PAH.

And here's the risk: forecasters give only a 30% chance for these projects to reach the market, despite their relatively advanced development status.

What does that mean for Actelion's valuation? and future?

Can you sense the "Nadare"?

Alexion Pharmaceuticals

Another company in this route is Alexion Pharmaceuticals. Their star drug is Soliris (eculizumab) for the treatment of paroxysmal nocturnal hemoglubinuria (PNH). As with most orphan drugs the target population of patients is relatively small, but each patient is worth a huge stream of euros a year. Soliris is their only drug in the market since its launch in 2007. So, in order to improve their future Alexion must extend and add more to their basket/ portfolio. The new nieche aHUS indication may not be enough.

So how about restricting the potential future competition?

Alexion's recent activity of acquiring Taligen for 111M\$ allows them control into Taligen's scientific lab that had been developing their key candidate TT30 as a potential rival to Alexion's drug eculizumab. Taligen's drug if reaches market, may extend Alexion's hold in the PNH nieche. PNH, causes immune reactions that attack and destroy red blood cells. There are only 8,000 to 10,000 people in North America and Western Europe with this rare blood disorder.

It's tough to tell how much money Taligen's investors will make from Alexion's purchase. With this purchase, Alexion may become a bigger spot on the M&A radar of big pharma. As its cash flow from new patients is positive, they have a longer breathing space (degrees of freedom) then other companies.

Can you sense the "Nadare"?

In conclusion, we find analogy between business situations and GO. We explained how high risk strategy is reflected by the avalanche joseki. When played well, the joseki leads to a "Win-Win" situations, otherwise – great loss.

Well, if you are into other businesses and interests, you may find and use the strategy game of GO as a tool to look at companies and evaluate their position and the road they are taking.

We highly recommend for pharma executives to study the game of GO, its finesse and benefit from the strategic tools and whole board (universal/ cosmic) view and thinking.

Decision making and positional judgment are in the heart of GO.

My experience from the history of the market is that most companies were able to recover and continue to lead the market. Following the patent losses, there is usually new growth emerging. Remember the Phoenix...

We will definitely see more mergers and acquisitions in the near future.

Further reading:

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Get Strong at Joseki vol 1– Richard Bozulich, Get Strong at Go series Vol 2, p. 2-3, Kiseido Publishing Company, 1995.

Even game Joseki - Nihon Ki-in, volume 5: p.8-14, Yutopian, 2003.

About the author:

Shavit Fragman is the President and CEO of MindPharma.

Shavit Fragman held senior positions in leading healthcare and pharma companies, consulted to multinational corporations.

He is a lecturer on strategy and involved in research in the cognitive field.

A former college lecturer on industrial pharmacy and formulations and form researcher in hypertension studies.

Shavit has been the president of the Israeli GO association for several years and organized the first 3 GO congresses.

Mind chain of GO clubs, managed by Shavit, promotes GO at a local and national level, encourages and support establishment of new GO clubs.



