THE BLACK SWAN CONNECTION

I was traveling to a micro-cap conference in Hood River, Oregon during the first presidential debate so outside of the soundbites, I missed the entire thing. Listening to some of the conference attendees the following day, it doesn't sound like I missed all that much. I recognize that politics has always been its own entertainment genre, but this year's episodes are particularly shocking. If I had a buck for every person I have heard say "are these two the best we have", I wouldn't have to schlep around on airplanes flying to investment conference trying to drum up interest in our website and this newsletter… That said, while I could not watch the debate due to my travel itinerary, I don't think the debate itself was even the most bizarre drama that oozed off of Capitol Hill this past month. In my view, the week's biggest political spectacle was the congressional hearing conducted to investigate Mylan Lab's price increases around its EpiPen. For edification, an EpiPen is a syringe full of epinephrine which is used to (immediately) treat people who are experiencing anaphylaxis, which in simple English generally means an allergic reaction.

Unlike the deeply partisan presidential debate and associated campaign(s), the grilling of Mylan and its CEO Heather Bresch, was a bipartisan love fest. It is rare indeed to see U.S representatives from both sides of the isle unite so vigorously against a common foe; a U.S corporation providing a drug that saves people's lives. Mylan employs 35,000 people worldwide, is the source of 1 in every 13 prescriptions written in the U.S. each day, and provides treatment for nearly half of all HIV patients in the developing world… among other nefarious deeds. That being the case, it's easy to understand their angry and united front. What's not the hate about a company doing all that awful stuff?

As usual the madness in this story lies in the "truth." Congress chose to berate Mylan and Ms. Bresch over the usual *aspects*, Big Pharma pillages the poor and the sick by providing treatments they must have to stay alive at exorbitant prices so executives and shareholders can get "filthy rich". Congress even managed to make an issue out of Ms. Bresch's $18 million salary, and the fact that she flew to the hearing in …God forbid…. A PRIVATE JET. With all due respect, if I made $18 million per year, I am not sure I would ever fly a commercial airline again either, but I digress.

As with many things Congressional, the absurdity of this most recent Big Pharma witch-hunt has a variety of levels. First, recognize that the genesis of Congress's Mylan wrath apparently stems from constituent complaints following Mylan's decision to significantly raise the price of their EpiPens. The logic there is clear, Mylan raised the price of a drug that people <u>need</u> to save the lives of their children **because they could**….and they have been doing it for years now. There are few alternatives in the marketplace (which we will address in a moment) so Mylan obviously

saw little market resistance to that approach. We are guessing they didn't quite anticipate the political backlash and there may be more than one reason for that.

Recognize, Heather Bresch is no stranger to politics. Her father is Democratic West Virginia Senator and former West Virginia Governor Joe Manchin. Many suggest Mr. Manchin's political position may have had something to do with his daughter's hiring and subsequent rise to the top of Mylan Labs. Needless to say, Ms. Bresch's various positions at Mylan for nearly a decade prior to assuming the CEO post in 2012 involved Capitol Hill lobbying efforts on behalf of Mylan's interests. The daughter of a powerful U.S. Senator lobbying for a major Pharma player in one of the country's most regulated industries. Employees don't get much more qualified than that. Make no mistake, Heather Bresch was a well known quantity in the FDA and pharmaceutical discourse of Washington DC long before she became the Mylan's CEO. We would argue that the results of that influence has something to do with Congress's recent distaste for Bresch and Mylan.

It seems that Ms. Bresch's father is not the only member of the family with some political clout. Apparently, Heather Bresch's mother (Joe Manchin's wife) Gayle Manchin was appointed to the National Association of State Boards of Education in 2012, where according to some journalists she "*spearheaded an unprecedented effort that encouraged states to require schools to purchase medical devices that fight life-threatening allergic reactions*". They also noted that these efforts *"helped pave the way for Mylan Specialty, maker of EpiPens, to develop a near monopoly in school nurses' offices. Eleven states drafted laws requiring epinephrine auto-injectors. Nearly every other state recommended schools stock them after what the White House called the "EpiPen Law" in 2013 gave funding preference to those that did"*. We aren't making any judgments one way or the other about whether or not Mrs. Manchin's intentions were to help school children or to help Ms. Bresch (her own children), however, regardless of the intent, Mylan, has clearly been the direct beneficiary of federal and state legislation effectively granting them a stranglehold on a market that the same legislation made much bigger by the same stroke of a pen. Ironically, 3 years later, the same legislators who helped her create that market power are chastising her for using it.

Meanwhile, some members of Congress levied a small piece of their EpiPen anger on the FDA. Their notion was/is that the FDA's approval process is too slow and too expensive for those developing new drugs and therapies. At least some of them got something right…another issue we will address more fully in a moment.

As unsettling as the above may be, the entire process has apparently missed at least one of the very big points in the whole EpiPen argument, which is the notion that without access to EpiPens, thousands of people, especially the poor who have been "priced out" of the EpiPen markets, are going to die. Whoa… hold on a second.

The American Academy of Asthma, Allergy and Immunology recently noted the following:

Anaphylaxis is a rapid-onset, potentially life-threatening systemic allergic reaction that can affect people of any age or sex. Current guidelines endorse aggressive therapy reflecting the

possibility that any episode of anaphylaxis has the potential to cause death. ***However, the actual risk of death is unclear***. (keep in mind anaphylaxis is what EpiPens mitigate).

In a recent article published in The Journal of Allergy & Clinical Immunology (JACI), Ma et al. examined the fatality rate among hospitalization or emergency department (ED) presentations for anaphylaxis and the mortality rate associated with anaphylaxis for the general population. This was a population-based epidemiologic study using 3 national databases: Nationwide Inpatient Sample (NIS, 1999-2009), Nationwide ED Sample (NEDS, 2006-2009), and Multiple Cause of Death Data (MCDD, 1999-2009). Sources for these databases were hospital, ED discharge records and death certificates, respectively.

The authors found that case fatality rates were between 0.25% and 0.33% among hospitalizations or ED presentations with anaphylaxis as the principal diagnosis. These rates represent a total of between 63 and 99 deaths per year in the US, ~77% of which occurred in hospitalized patients. Rate of anaphylaxis hospitalizations rose from 21.0 to 25.1 per million population between 1999 and 2009. However, overall mortality rates appeared stable in the last decade and ranged from 0.63 to 0.76 per million population (186 to 225 deaths per year).

These results suggest that the overwhelming majority of hospitalizations or ED presentations for anaphylaxis did not result in death, with an average case fatality rate of 0.3%. Nationwide, despite the increase of anaphylaxis incidence, it is also reassuring that mortality rates associated with anaphylaxis have remained stable in the last decade and were well under 1 per million person-years. Both these observations likely reflect the quality of care that can be provided in the urgent care setting. ***Although anaphylactic reactions are potentially life threatening, the probability of dying is very low****, especially for those cases that involve ED or hospital attention.*

To be clear, we are not minimizing the threat that anaphylaxis poses to people with acute allergies. I have members of my immediate family with allergies who by the way own EpiPens. However, if the above data from The Journal of Allergy & Clinical Immunology are accurate, and we know for example that the EpiPen is a "billion dollar drug" for Mylan, then the math suggests that we may be spending about $5 million per year per person to save those same 186-225 people from anaphylaxis death. If we consider that Mylan's $1 billion in assumed revenues, represent only the whole cost of the drug, then the cost could easily be closer to $10 million per person. To put that into perspective, ALS (Lou Gehrig's Disease) is diagnosed in about 5,600 additional Americans each year. That makes it relatively rare in terms of many diseases. There is no known cure, so while drugs have been keeping ALS patients alive longer than in the past, virtually everyone diagnosed with the disease will die from it typically with a handful of years (provided something else doesn't kill them first). Statistics suggest that ALS kills about 20 in 1 million people, while anaphylaxis kills less than 1 per million people (specifically, .63 to .75), which suggests that the average person is 27 times more likely to die from ALS than from anaphylaxis. The ALS association suggests that they have committed more than $67 million to find treatments for ALS, which is a lot of money. However, if the same $5 million per annual "fatality" was spent on ALS as is apparently spent on anaphylaxis, we would be spending $28 billion per year curing ALS. I am not a scientist, and maybe there is no cure for ALS, but my

sense is that if we were spending $28 billion per year trying to cure it, we probably would have by now.

So here is my point, what has *really* happened here is that the US Congress, state legislatures, state school boards, schools, public facilities and the public itself have been lead to believe, largely by Mylan's brilliant marketing efforts, that anaphylaxis is an epidemic with a simple, low cost, highly portable, use anywhere by anyone solution; the EpiPen. Who can say no to that? Because of Mylan's lobbying and the resulting federal EpiPen Law, at least 11 states require schools to keep epinephrine on hand. In addition, the federal government provides incentives for schools to stock the product. In addition, some states require that the epinephrine be delivered by an "injector" as opposed to a stander hypodermic needle. That requirement favors Mylan's version of epinephrine delivery injector…imagine that, it's almost like Mylan helped write the law (actually, some suggest that they actually did)

Look, I have no problem with Mylan doing what it can to enhance its revenues, operating results, shareholder value etc. Even to the degree that it involves lobbying Congress to help them get there. My problem lies in Congress's willingness to be a part of it, and ironically, its anger over a mess they have helped create. Worse yet, they are now using their bully pulpit to call down Mylan for a situation that essentially stems from a lack of market competition (Mylan controls about 90% of the market), which oddly enough is also something Congress has had a hand in. Enter: **Adamis Pharmaceuticals Corporation (NASDAQ CM: ADMP).**

Adamis Pharmaceuticals is a San Diego, California based "specialty biopharmaceutical company". The Company has among other things, been working on a low cost pre-filled epinephrine syringe. They have been working on getting it approved by the FDA for over two years now. In June of this year, the stock was cut in half after the Company announced that it received a letter from the FDA requesting expansion of *"its human factors study (patient usability) and reliability study (product stress testing)".* Adamis has been jumping through FDA hoops since submitting the NDA in May 2012. Keep in mind, the Adamis product is filled with epinephrine. Epinephrine has been used as a treatment for over 100 years. The second part of their product is essentially a hypodermic needle. Those have been around longer than epinephrine. Adamis simply wants to pre-fill the needles and ship them out the door providing a safe, low cost competitive alternative to the EpiPen. If the U.S Congress wants to blame Mylan labs for owning a 90% market share and as a result pricing their product anywhere they darn well please, I suppose they can do that. However, as some members of Congress correctly observed, the real problem here is a lack of competition, giving Mylan almost complete pricing power. Interestingly enough, the FDA seems quite content to kick the can down the road with questionable questions regarding the approval of competing drugs. If Congress wants to know why Mylan can raise EpiPen prices indiscriminately the answer is, "no competition". If the FDA wants to know why there is no competition, they should ask themselves, or at least their cohorts at the FDA, because they have had the power to approve more competition for the EpiPen for quite some time now, but each competitor seems to encounter another hitch in the process. I submit, that view is completely anecdotal, but it's curious nonetheless, since again, we are

dealing with a drug (epinephrine) and technology (a hypodermic needle) that have both been around for well over a century.

In the big picture, Adamis is hardly the first small company to encounter the FDA's moving target of challenges. I would venture to say that most microcap and/or small cap followers who have been around for any measurable period of time can recite a handful of FDA rejection stories. In fact, in most cases, those people probably still don't fully understand what it was the issuers failed to provide. If that sounds a bit "Trumpesque" (the system is rigged…) it's because it is.

I understand the critical need for safety and efficacy in the nation's pharmaceutical and device industry, but it often looks as though the FDA's primary criteria for proving up those notions starts with the expenditure of exorbitant amounts of money. Make no mistake, the FDA's expensive clinical trial protocol(s), is a clear a barrier to entry that on the face makes the pharmaceutical and medical device industry less competitive. Again, I am not suggesting that the approval process should be a rubber stamp, but it needs a serious overhaul. Moreover, the cost of clinical trials effectively locks out a number of promising technologies that have the potential to save lives, lower medical costs and provide various other societal benefits but never see the light of day simply because of the costs associated with clinical trials and other FDA protocols. Here are just *a few* examples beyond Adamis (there are myriads more) that come to mind.

Integrity Applications, Inc. (OTC: IGAP). Integrity has a non-invasive device which clips to a patient's earlobe and reads their glucose levels. Most diabetics currently stick themselves with a needle a few times a day and apply it to a test strip. The company has tested, retested and calibrated the device to death and has been given approval to sell the device in Europe and several other reciprocal nations around the world via a "CE Mark" approval, which is somewhat similar to an FDA approval in the U.S. The company recently submitted a "pre-submission" to the FDA to learn what sort of trials the FDA will require. Translation: more time, a lot more money, less competition and fewer choice for diabetics. Why does a device that clips to someone's earlobe and has obvious benefits for millions of Americans (estimates suggest there are nearly 30 million diabetics in the US alone) require more of the same tests and the same data but compiled *exactly* how the FDA wants it? It's like a game of Simon says.

Aethlon Medical, Inc. (Nasdaq CM: AEMD). I have followed Aethlon for just about as long as I can recall. The company has developed a product they refer to as the Hemopurifier, which in simple terms is a blood purifier that is administered much like dialysis. (The Company has some additional technology as well.) The Hemopurifier is effective in filtering viruses from the blood and reducing viral load allowing the immune system to overcome the ravages of viral infection on its own. (Most viruses don't kill people they just suppress the immune system so much that something else kills them). Like most small biotech's, Aethlon has its sights set on FDA approvals, which carries a large price tag. Technically, they will need FDA trials for every indication of the device. That is, a trial for Ebola virus, a trial for Zika, a trial for Bird Flu a trial for Dengue…you get the picture**.**

In 2014, amidst the Ebola outbreak, doctors in Frankfurt, Germany were faced with the task of treating a Ugandan doctor who had contracted Ebola. When they decided to deploy the Hemopurifier (as a bit of a last resort), the patient *"needed a ventilator to breathe, and as the virus ravaged his body, several of his organs, including his kidneys, failed. The medical team placed him on dialysis and hoped for the best"*. Following treatment with the Hemopurifier, the patient was later released from the hospital…healthy again. Moreover, Aethlon notes that *"to date, Hemopurifier therapy has been successfully administered in approximately one hundred treatment experiences in health compromised HIV and HCV infected individuals"*.

It's odd to me that Aethlon will need to spend millions of dollars (which it doesn't have on hand) on MORE "clinical" evidence to get an FDA approval to save people's lives. People who are being compromised by Zika (among other viruses) should be wondering the same thing…with far more urgency.

Lastly, **Volition Rx Ltd (NYSE Mkt: VNRX),** is developing diagnostic (blood based) tests for cancer. Like the others, they need to get FDA approvals to sell the product(s) in the U.S. As with many of the others, the Company has sought (and achieved) CE Mark approval in Europe as a means of first establishing a commercial business. They are starting with colorectal cancer but their technology is applicable to a number of others. Their blood tests ("liquid diagnostics") reflect marked results in identifying potential cancer concerns. Today, the U.S. health system's 'standard of care" for colorectal diagnostics is a colonoscopy. In the U.S. people get a colonoscopy when they turn 50 years old at a price tag of several thousand dollars. By the grace of God, a very small percentage of those tested actually have a serious problem. Volition's test could be an initial test eliminating the vast majority of those colonoscopy's performed, saving millions and millions of U.S. healthcare dollars each year. Instead, Volition will need to provide the FDA with what is essentially a new set of results from tests they have already successfully run in order to get approval and ultimately benefit the U.S. health care system with much needed savings. We are wasting U.S healthcare dollars in the name of upholding the FDA's self-proclaimed "gold standard" qualifications.

At this rate, the U.S. will soon end up with the "best" health care system that nobody can afford. That is, if we are not already there. In the meantime, promising technologies will continue to fail because they can't raise the money to pay the FDA toll. If Congress wants to pound the table and make a difference, they should probably start there.

Dave Lavigne
Editor – Stock Market Manager