INTEROFFICE MEMORANDUM

TO: MARC SCHNEIDMAN, AQUILO CAPITAL

FROM: JOHN P. MCCARTHY

SUBJECT: TWENTY GOOD QUESTIONS

DATE: DECEMBER 2, 2020

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1. **Has medical research neglected virology in recent years?**

No, medical research has not moved away from virology, but the majority of work is being done in academic centers, not industry. However, biotechnology and pharmaceutical companies have not entirely abandoned the therapeutic space. For example, Hepatitis C was a major success and Hepatitis B is now attracting tremendous interest and effort. There are other viruses that have attracted the interest of some of the big vaccine players.

2. **Do you prefer to invest in technology platforms to discover new therapies or the therapies themselves?**

We start with platform companies first which we believe provides the margin of safety and gives our investments a significant competitive advantage. We invest in platforms that have demonstrated an ability (or at least strong evidence) to generate novel therapies. All of our companies have a large portfolio of therapies in various stages of human testing BUT at the core is the platform. Besides for the downside protection, companies with a novel platform can expect a higher ROI if they can recycle revenue and earning back into the discovery of novel therapies.

3. **What are some of the main differences in how American and European regulations differ for drug discovery and thus how biotech companies operate?**

Over the past decade we have seen an increased harmonization between the US FDA and the European EMA. There can still be discrepancies on individual drugs but it is becoming much less common. In both arenas, drugs are based in their efficacy and safety and the risk/reward versus the current standard of care.

4. **Are there many intangible assets or goodwill in the businesses you research?**

Definitely. There is a premium placed on quality management, domain expertise, trade secrets and overall intellectual property. Management teams who have a history of successful M&A are often trading at premium to their peers.

5. **Speaking of intangibles, how do you view intellectual property when valuing opportunities?**

When investing in novel therapeutics our working assumption is there is good composition of matter on the individual molecules. We diligence to verify the patents are indeed in place. The IP on the platform can be trickier and often times know how and trade secrets are equally important.

6. **What "orphan drugs" (defined by FDA as affecting less than 200,000) are going to really show progress in the coming few years?**

With the rise of gene therapies, many orphan diseases can potentially be addressed. Our hope is the CNS (Central Nervous System) diseases, e.g., trinucleoside repeat disorders like Huntington disease will be better addressed in the near future.

7. **What large, serious disorders are going to see effective therapies in the coming few years?**

NASH (Nonalcoholic Fatty Liver Disease), Hepatitis B, RAS driven cancers and multiple autoimmune disorders. ((KRAS, NRAS, and HRAS) is the most frequently mutated gene family in cancer.)

8. **Are there negative externalities from biotech production?**

"Financial toxicity" to patients is one, like bankruptcy. There may be broader environment implications to a growing biotech industry that we do not completely understand.

9. **Are there companies in this space, which in your view, walk an ethical fine line?**

There are many specialty pharmaceutical companies with old drugs and high and rising prices. These companies rely on legal loopholes, like REMS, to fend off competition and maintain exorbitant prices. (A Risk Evaluation and Mitigation Strategy (**REMS**) is a drug safety program that the U.S. Food and Drug Administration (FDA) can require for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risks.)

10. **If you could do one thing to lower the cost of health care devices or therapies, what would you do?**

For therapeutics, one answer would be to more widely adopt a pay-for-value pricing strategy. Of course this can be tricky to implement as each drug would need a metric to monitor effectiveness over time.

11. **How is Artificial Intelligence affecting drug discovery?**

At the moment more smoke than fire with AI in drug discovery. Perhaps too early in the cycle to know the value. What is true is that it's nearly impossible to diligence AI strategies.

12. **What areas of biotech are very popular with investors and what areas are not very popular?**

The hot areas remain immune-oncology especially the heme-oncology arena, metabolic disease (NASH and obesity), and orphan diseases in almost all areas. The not so hot include, tropical diseases, general pain and anesthetics and certain viral diseases like prophylactic HIV.

13. **A "common wisdom" seems to be that large cap pharma have evolved toward marketing and away from original research. Is this perception correct?**

Broadly yes, but we may still be in the early days of the decoupling of commercialization from research. There is still early R&D inside large cap pharma and significant human capital although at a significantly reduced scale from just a few years ago.

14. **How do you differentiate between a biotech company in temporary trouble versus fundamental trouble?**

We invest in companies with four key pillars; financial strength, platform technologies, pipelines and partnerships. When a pillar disappears we believe there is a greater chance of near term fundamental trouble. If the pillars are intact, but the companies stumbles with a single drug, the problem is likely temporary.

15. **In biotech, are markets less efficient where price moves away from value and, if so, why is this the case?**

Yes, given the complexity of the science and technology and the fact, standard financial metrics of value seldom apply, the gap between price and value can grow wide for sustained periods

16. **Is Precision Medicine, customized by patient, something that can be widely affordable?**

I can imagine a scenario where it could, provided the clinical outcomes are exceptional. CAR T therapies are not widely available, but one could envision economics of scale to make it work. The bigger issue is: not all diseases are amenable to a patient specific drug approach if the disease is driven by multiple or complex mechanisms of action (which are most). (Chimeric antigen receptor T cells are T cells that have been genetically engineered to produces an artificial T cell receptor for use in immunotherapy

17. **Any attitudes you seek when underperforming or outperforming your index?**

We try to stay disciplined and focused on our fundamental value investing methodology. Our focus is on long term, risk adjusted, absolute returns, not short-term volatility. Our process and investment philosophy is to take advantage of short term volatility to deploy capital. We have a strong

understanding of the value of the companies and short term spikes in volatility, dislocations in the market or big drawdowns are precisely when we are most active investing. Relative returns are a distraction.

18. **Does the FDA drug approval process now move faster or slower than ten years ago? If you could improve the process, what would you do?**

    a. Faster in many circumstances given the increase in orphan disease and mechanism-driven targeted therapeutics.
    b. Aside from more government appropriation to FDA for more application and site reviewers, I would like to see a measure that lowers the likelihood that companies fail to meet necessary standards for good manufacturing practices, which includes a detailed plan earlier in development. If implemented, this would avoid a substantial number of delayed approvals.

19. **How have you changed your security screening process in recent years?**

Refined, not changed significantly. Most of our new opportunities often come from existing diligence project already underway.

20. **What have you learned from investing that might broadly be called a "life lesson"?**

Trading stocks is not investing. Cycles in history often repeat themselves. Patience is a virtue. Long-term capital is a huge competitive advantage. Avoid the crowd.