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PM Corner: A Conversation with RA Capital's Peter Kolchinsky

We are continuing our series of discussions with leading healthcare and biopharma portfolio managers as we try to leverage the top minds in the investment industry to help inform our own views in this rapidly changing biopharma era.

RA Capital is one of the leading dedicated healthcare investment funds and has been built over nearly two decades with a unique approach to analyzing therapeutic categories. Our conversation spans a range of topics including RA's well known TechAtlas, the drug pricing debate, newco idea generation and company formation, surviving in this era of hyperinnovation, and much more.

(For our previous "PM Corner" conversation with Rod Wong, click [HERE](#)).

Question: Tell us about RA Capital's history and how it's evolved as the sector has evolved (more science, more companies).

Currently, RA Capital manages over \$3B, employs around 80 people, and invests in public and private companies, mostly focused on drug development but including some medical devices and diagnostics. We also form our own companies from scratch. But all that is a far cry from how we started...

[Click on note for full conversation](#)

RA Capital's history/evolution continued...

- Raj and I got our start investing in public biotech companies in the early 2000s. We had science backgrounds but no finance experience and focused on development-stage drug companies. In our early years, the industry was still recovering from the collapse of the genomics bubble, so there were a lot of “re-plays”: reformulating, repurposing, relocating, and repricing (price-jacking). We weren't often obligated to dive into the nitty-gritty specifics of, say, GLP tox data, which is good because we didn't have drug development experience. But over time, the science we were exposed to deepened and we learned to dive more deeply.
- From the beginning, we compensated for the little information we could glean from any single company in a given space by talking to all companies in that space to triangulate on deeper underlying truths. We would tour every disease area with an open mind, hearing out every company. So we might start off thinking one company was a good investment and come to appreciate that another was even better.
- We now have a lot of capital to deploy, a great team, plenty of knowledge and the bandwidth to process a lot more, and the flexibility to invest in publics, privates, and newcos all in the same portfolio at a time when biotech has really hit its stride.

Question: RA Capital is well known for its disease maps. What can you tell us about these?

- Keeping track of our diligence in long, written notes became inefficient, and we discovered that it was more efficient for us to communicate using **visual mindmaps**. This eventually led us to create an internal division focused on competitive landscape mapping known as **TechAtlas**. Our TechAtlas team enables us to digest an incredible amount of data, contextualize it, and distill it down to critical insights that guide our investment decisions. Today, we typically host 8-10 biotech companies in our offices each day, 40-50 per week, and in parallel are evaluating scores of academic projects, speaking with various experts to help with diligence, etc. That level of input would have paralyzed us back when we were running an old-school process. Our current diligence framework is essential to preserving our decisiveness amidst all the information flow.
- Once we starting mapping, around 2011, our maps also helped us see each drug as a chess piece on a board. We could see gaps in pharma companies' portfolios and deduce which smaller companies could fit where. Over time, we began to understand pharma better and became more patient in waiting for the acquisitions that the logic of our maps deemed inevitable. Sometimes we had to wait a long time and sometimes the acquisitions never happened, but our maps were correct often enough. Holding

companies longer for higher upside became important as our assets grew and liquidity became limiting.

- TechAtlas is not only the knowledge core of our firm but also the farm team for our investment team and portfolio companies. We teach our associates how to do effective diligence and quickly become expert-enough in any field to make intelligent decisions. They learn to think strategically, and that's useful no matter what they go on to do later.

Question: When, why, and how did you add private company investments to the mix?

- Around the time we started up TechAtlas. Although our strategy at the time was focused on investing in public companies and therefore to us private companies were merely their competitors, we weren't blind to the fact that some of these privates were doing great things and seemed like they would go to become valuable public companies. So we got permission from our LPs to expand to investing in privates, but from the same fund. We use side-pockets to match the liquidity of the portfolio with the liquidity our LPs have so that LPs can redeem what's in the public portion of the fund without impacting other investors' exposure to privates (without side-pockets, redemptions would increase the exposure of remaining investors to illiquid private positions). We made our first crossover investments in 2012, around the time this style of investing was first emerging and have been pretty active since.
- Investing in public and privates with one unified strategy from the same fund is core to how we operate. That's not unique, but it's rare (many other funds have separate public and private investment teams and funds, sometimes even with communication barriers between the two sides). We want all of our firm's knowledge and efforts focused on one portfolio. As private companies go public, they simply transform but remain within the same portfolio, freeing up capital for us to make new private investments. In a sense, investing in privates is like planting seeds that blossom into public positions. These days, most of our public exposure happens to be in companies that started as private investments, though we frequently will invest *de novo* in public companies.
- And while we now have a separate venture fund we call Nexus, that fund still invests in all the same private companies that our main evergreen fund invests in and is managed by the same team. It's a source of more private capital rather than a separate strategy.

Question: How have your private company investments changed your view of the field?

Serving on the boards of private companies taught us a lot about what it takes to build companies and constantly problem-solve. The public markets don't get to see how the sausage

is made, which is just as well because it can be harrowing. But we have come to appreciate the way driven, talented people can work through most any challenge to keep programs going. Now, even when we're not on the board of a public company but know they have great people, we have more confidence that they can solve problems behind the scenes. That makes us more patient public investors. Also, as our network, footprint, experience, and assets expanded, we realized that we had the three key ingredients that we needed to start our own companies: intellectual capital (TechAtlas), human capital (our network), and financial capital. So we dove into the deep end of the pool.

Question: How does RA Capital tackle new company formation?

- For the last several years, we've been incubating a company formation/building initiative led by Josh Resnick and Andrew Levin. This team includes people we've promoted from within TechAtlas, very talented people we have hired from outside, and executives of former portfolio companies who we've long wished to work with more closely. Each person is typically involved in multiple projects. When one works, they shift more time there. When something isn't working out, there is always something more compelling to shift to. We're tackling white spaces on our maps and there is a lot of them.
- We've got people out in the field building relationships with academic researchers, we're engaged with pharmas to spin out attractive programs, and our team is tinkering with its own novel molecules. I never imagined that RA Capital would have patents to its name, but we do (all assigned to newcos). And what Raj and I are really proud of is that while we recruited these great, earnest, hard-working, creative people and gave them the resources and encouragement to take us in this new direction, they ran with it and independently built something beyond our expectations.

Question: Your website says that you try to provide more than capital. What does that mean and why do you do it?

- It's amazing how many smart people have compelling ideas for how to permanently upgrade human health, and it takes so much to realize those ideas. The question we're always trying to answer is "What would make great companies choose us as their shareholder?" So we study all the problems that innovators have and figure out how to systematically be of greatest service possible to them as they build their companies and pursue breakthroughs. If they need our maps, we're happy to share. If they need help digesting a ton of literature or talking to a bunch of KOLs to decide whether to expand into a new therapeutic area, we have the bandwidth to help. If they want introductions to potential partners or help recruiting executives, we'll gladly turn to our network. We can help a company run a financing process by building a syndicate of our peers, whether a private one or even an IPO. Our graphics team has even developed beautiful slide decks for our companies. The list goes on.

- And when one of their drugs gets on the market and starts helping patients, that's a remarkable moment... to know that we made some small contribution to permanently upgrading human health. That's why I got into biotech. Not every job offers those moments. We're lucky to have that.

Question: How does the size and structure of your team help you manage all the information flow? Do you still go as deep into companies as you used to?

- On one hand, we have a large team and therefore typically have the bandwidth to perform diligence on almost any company at any time. But at the same time, we know that it's not productive to have an analyst take a random meeting with a company working on something unfamiliar. Raj and I grew up with the old school approach. We simply met with so many different companies, scrambling to make sense of them as best we could, that over time we developed a working knowledge of many therapeutic areas. But that took years. We didn't think it would be efficient to expand our team by putting everyone we hired through that.
- Today, most of our new hires start out on our TechAtlas team and might be assigned to work on a given disease such as lupus. Within several months, an associate will become an expert on lupus. There may not be investment opportunities in lupus for a while, so that person won't have much direct investment analysis to do and will go on to cover other areas, but when a lupus company crosses our radar, that person has the expertise and bandwidth to take a meeting and really get into the weeds quickly. It's great to see how someone less than a year out of school can confidently engage in diligence with a team of senior executives in their field. That associate won't be confident evaluating a company in a different space, but, having once attained an effective level of expertise, they will trust themselves to climb that learning curve again and again. That's the confidence and capability we strive to instill in all of our hires as quickly as possible. After many years, collectively, our TechAtlas team is expert in many areas, and we have bandwidth to assign the right person to just about any company.
- Our investment team consists of people who have been doing this long enough that they can shift their attention across many therapeutic areas, though people still tend to have areas of expertise. But we try to avoid asking anyone to focus their time in any one area. We don't want anyone recommending an oncology investment because all they know is oncology. Those members of our investment team who happen to have more oncology experience should be recommending an oncology investment because it's the best investment they can find at that time across all therapeutic areas, not just the best one in oncology.
- It takes a while for a member of the TechAtlas team to develop that breadth, but after rotating through a number of domains such as oncology, neuro, orphan, cardiac, and psych,

people tend to develop a generalized pattern recognition that lets them work in other areas, especially when they can rely on colleagues with complementary expertise. TechAtlas is constantly teaching our investment team about what's going on in every therapeutic area—how the standard of care will change with every positive clinical trial result; which companies' programs may be validated or invalidated by the results of related programs; and how different therapeutic modalities might impact one another, to name a few examples. And those teaching sessions are also a great way for the people in TechAtlas to learn because they are bombarded with incisive questions by our investment team and get to see how we reach a decision regarding what to focus on.

Question: How do you choose which companies or fields to drill into?

- When you add up all the potential opportunities out there – publics, privates, whitespace newcos, pharma or academic spin outs – the flood of opportunity may seem unmanageable. TechAtlas gives us an operational framework for handle and analyze opportunity systematically and efficiently. We're always mindful of the risk that we might overlook a great investment and are constantly refining our methodology to minimize that risk. For example, because we have someone tracking everything that's going on in lupus, we know which companies in that landscape are working on something potentially compelling. Either we'll reach out to those companies about financing them, even if they aren't talking to investors yet, or, when they reach out, we'll know to assemble a team of people, including senior members of our investment team, to get a deep update and make a rapid decision.
- If a company we haven't heard of with a lupus program suddenly appears on our radar, our TechAtlas lupus expert will typically take a first meeting or call to rapidly put what that company is working on into context and make a case to our investment team whether, why, and how we should prioritize further diligence. The point is that we're all awash in a tremendous amount of information, but it's useless without context. So the TechAtlas framework restores important context to the deluge of data and turns it into actionable knowledge that keeps us quick and decisive.
- Of course, we're also old school in some ways—if someone we know and trust tells us that a company is great, we might ask a member of TechAtlas and a member of the investment team to meet with the company together so we can come to a decision faster.
- On the public side, since there are a manageable number of opportunities, we track which companies will generate what data when and prepare scenarios of how every trial might read out so that we know which course of action we're likely to take. Sometimes the outcome is different than we planned for and we have to scramble, so we do.

- Some days push us to our limits, so we continue to expand our team and refine our methodology to be more effective and efficient so there is never a time we have to turn down the chance to do deep diligence because we're overstretched.

Question: Heading into an election year, how are you positioning with biotech, especially in light of the noise around drug pricing?

- That's something we get asked a lot so I'll offer the same answer we usually do. Biotech is the area where we see the most promising innovations that will dramatically improve patient lives. We are actually curing some diseases or turning terminal illnesses into chronic conditions that can be managed while maintaining a high quality of life. In exchange for a life transforming innovation, a drug company is offered a temporary pricing monopoly in the form of patent protection to recoup its investment. When the patent expires, this innovation goes generic and becomes a public good, with pricing going down more than 90% for many small molecules. We don't think anything that comes out of Congress will actually shut down an industry that does so much good for society and that America excels at.
- What some politicians and the public currently miss is that drugs going generic is the price control we've long had and the only one we need. Outright price controls on drugs would indeed make today's drugs cheaper for patients and society but would also shut down investment in new treatments, which would halt the expansion of our already vast armamentarium of generic drugs. Tomorrow's healthcare would then be no better than today's. And yet, we can still do so much with the biology we understand and the technologies within our grasp.
- We believe that enough people within the US government appreciate this logic that, regardless of the aggressively anti-pharmaceutical headlines that rotate through the news cycle, today's withering rhetoric will not translate into innovation-destroying policies, though I do think it's important that we all continue to make this case to the American public and Congress.

Question: What do you see as the biggest risks/opportunities for the sector?

- I think that the risks of drug development are shifting from probability of technical or clinical success, which quantify the risks of – for example – a clinical trial failing, to those of strategic complexity. Historically, the chessboards have been so empty that making any drug that works has been considered a win. However, with more and more drugs coming to market, it's no longer enough to make a drug that simply works. You have to make a drug that actually sells. Perhaps you're painstakingly carving a RORyt inhibitor bishop in the hopes of

placing it on the psoriasis chessboard. But will that piece be necessary or valuable in the context of a Tyk2 inhibitor queen?

- With all this strategic complexity in so many therapeutic areas, even in orphan diseases, successful companies have to correctly answer this question: Of all the things they can do, what should they do? For us, the TechAtlas team we've built and the massive library of maps we've created are our homegrown response to this increasing problem of strategic competitive complexity.
- For example, when we invested in Synthorx, which uses non-natural nucleic acids to encode special proteins, our TechAtlas and investment teams evaluated dozens of applications and ultimately advised the company that cytokines would likely be fertile ground and stand out from the fray in immuno-oncology. The management team instantly saw how good the fit was between their existing capability, which allowed them to site-specifically glycosylate proteins, and the problems that needed to be solved with cytokines, both in terms of half-life extension and shifting receptor selectivity. So the company pivoted to that target class. That exercise—matching the problem to the tool—involved more than half of our team across dozens of therapeutic areas. Small companies rarely have that bandwidth and therefore I fear they are increasingly likely to discover that, even if they succeed in making the drug they want to make, it won't be relevant by the time it comes to market.
- To use a hockey analogy, they will be skating to where the puck will have been, not where it's going to be.

Question: What is the objective of the new Nexus fund?

- Our main fund, which holds most of our capital, can devote a certain percentage of its assets to private investments. That means that sometimes the amount of capital we can deploy into private companies can be constrained if there is a drawdown in public, such as during a market correction. So Nexus gives us a steady pool of capital we can draw on at all times to continue to make private investments at a steady pace through all market conditions, with Nexus investing more when the main fund is constrained. That allows us to be a more reliable source of capital for private companies and aligns with our mission of being a constructive, preferred shareholder for great companies. But launching Nexus doesn't change our strategy in any major way. There won't be any types of companies that we will invest in now that we couldn't or wouldn't have invested in before Nexus. We were doing venture investing long before Nexus launched.

Question: Are you concerned the industry isn't returning capital to investors (outside from limited M&A)?

- I think things are pretty much as they should be and certainly better than they were over a decade ago. Pharma is returning tens of billions of dollars back to investors through acquisitions of smaller companies and we are happily reinvesting tons of capital back into new companies. They also pay dividends. So I think there is a good balance of present returns and investment in future returns. I think that companies like Exelixis, which have been prudent and deliberate in considering how to invest the rewards from their huge commercial win, have clearly learned a lesson from companies like Cephalon and Sepracor that aggressively reinvested their gross profits into pipelines that their shareholders didn't believe in (thereby depressing their stock prices to levels that allowed acquirers to swoop in). Activists help bring discipline to companies that might not be redeploying capital judiciously.

Question: Are you still participating in IPOs? How often do you participate if you weren't in the crossover/earlier rounds? How often when you were in the crossover/earlier?

- Yes. We're happy to take a position in a great company at a good price at any time, whether in a private financing, IPO, or on the open market or in a follow-on financing. We honor our commitments to our companies and, if we participate in a crossover round, we know that as long as the plan remains intact and on track, it's our job to help capitalize that plan by ensuring that they can crossover smoothly via an IPO.

Question: Is there a 'sweet spot' in biopharma today for investments (stage of financing or valuation range), and if so, where do you think that is?

- We see a lot of great companies at every stage and across many valuation ranges. I can't define any sweet spots and haven't found it productive to try, since they are always changing as people flood into yesterday's sweet spots. I would have said in the past that we didn't look at companies over \$5B, but even that has changed. We now see opportunities to build more companies like Vertex.

Question: Do you think biotech public markets are still efficient? Does your Series I financing proposal presume they are? Latest thinking on Series I model?

- Biotech markets have never been efficient and certainly aren't now.
- In terms of pricing deals, we know that companies underprice truly oversubscribed rounds, which means they fail to discover what price some of those funds would pay to get larger orders. For example, even if one fund offers a higher price for a full allocation, the banks will

then offer that higher price to others and then still allocate broadly, cutting the original bidder back. By treating the funds with the highest conviction as stalking horses to extract higher bids from all bidders and then allocating to all the banks' trading accounts, bankers aren't giving any investors a real incentive to compete for an allocation that way that they naturally do in private financing term sheet battles.

- The current convention is good for all the traders who get small allocations in those deals and flip them higher, but it comes at the expense of both the company and the fundamental investors who really want to own that company for a longer run of value creation. I'll still buy those shares on the open market, but now at higher prices. I may as well have just paid that higher price to the company, but it seems pointless to let all the traders arbitrage inefficiently priced IPOs. So yes, there is a more efficient way to do IPOs and follow-on financings that is better for companies and their major shareholders.
- A handful of our companies have done financings using a more structured, rules-based approach (check out the data-packed Series I deck on our website). IPOs that have been tightly allocated to investors who clearly want to hold unflappably large positions have held up, even in tough markets. That's no surprise. It's logical. When you do a financing based on logic, you get a logical outcome. When you do it based on the conventional process that encourages investors to lie about how much they want as they guess at the degree of cutback so they end up with a small allocation that they intend to flip, then you can't be sure of the outcome.
- Banks might not like the rules-based approach we're advocating for, but they have to acknowledge that they serve the company, even if some banks may wish to serve their other clients at the same time. The ones who lose out in this new process are the traders. Maybe being cut out of the process will incentivize more traders to amend their strategies and become more fundamental shareholders. That would be good for companies and I could certainly respect having more such competitors. But I definitely don't see the merit of bankers cutting fundamental investors back to make room for traders who everyone knows will turn right around and flip those shares back to the fundamental investors.
- Some people think it's good to have liquidity, but that's just pointless liquidity. The liquidity you want is the liquidity you get when more investors recognize that a company is a bargain at higher and higher prices, paying up more such that current shareholders are compelled to trim their positions and therefore create an opportunity for the company to expand its shareholder base. But liquidity at or around the price of a financing achieves nothing except to correct allocation mistakes that should never have been made.

Question: You recently launched Carnot, an incubator for early stage biotech. Tell us about this element of RA capital. Advantages/disadvantages of having an incubator approach?

- The advantage is that you can act on ideas when there is no company to invest in and test these ideas out incredibly quickly and efficiently. You can fill the white space and create the investment opportunity yourself. It's nice that when you do that, your cost basis is zero. You own the whole company. The disadvantage is that it takes a great deal of effort to remain dispassionate about your own newcos, especially when they depend entirely on you.
- We're used to the tension of investing in companies—they think they are great and we make up our own minds. That's a healthy tension and if we pass, those companies might raise money from other investors. They still get to pursue what they believe in and we may have a chance to invest in the future.
- But a newco that's been formed by our colleagues depends on us. If we change our mind about it, it's unlikely that someone else will want to invest. So when we say "no, we don't think that's a good investment," we're likely condemning that project. We try to get to a yes and we're transparent in our thinking to give the people championing the newco a chance to spot our errors in analysis and correct them, but if our investment team remains unconvinced then we won't fund the newco. The worst thing about that is that we have to live with the reality that we may never know what it could have become and won't get another chance to invest later, when it's been derided, because the idea likely won't get funding from anyone else once we've passed on it.
- In most of our company-creation peers, the company builder who has to figure out "how do I make it work" is also the same person who assesses "what is it worth if it works" and "what is the probability of success". There is a risk of confirmation bias that can result in a company appearing to be doing well and enjoying a healthy valuation until it faced the independent assessment of the public markets. Our strength is that we are able to apply our more public markets diligence process right at the point of the very first experiment.
- We involve our investment team in the newco ideation process from an early stage so that the people conceiving the newco have the benefit of knowing whether they are getting "warm" or "cold." A huge advantage to that is that those of us used to just deciding whether we like an existing company with a polished slide deck are getting to participate in the process of creatively shaping a company from scratch. Judging an existing slide deck is entirely different from creating one from scratch. And the company creators on the team are getting the benefit of the objective assessment a seasoned late-stage investor from day one. And this new experience is also helping our investment team to see where there is an opportunity to evolve some of our existing, more mature companies. In reality, all

companies are in the process of being formed to various extents. So there is some element of incubating and ideation that should be applied to all companies.

Question: How do you find the people for your new companies?

- When you have an incubator and are building companies, you're always hungry for great people. Before we had an incubator, we looked at fellow board members as colleagues we were content to see in the context of those particular board meetings. Now that we have newcos to grow, we hunger for their expertise and bandwidth and are always thinking about how we're going to recruit them. When we know one of our companies is going to be acquired, we start planning how we're going to court its best people to bring into all the projects we're cooking up. I love that company creation— including the incubator - has given us this extra motivation to productively harness the talents, creativity, and drive of the people around us and to attract more people to our ecosystem.
- For example, we hold conferences for board members of our companies where we share data-rich analyses of topics such as financings, compensation, and governance that directors are grappling with. Ever wonder which sell-side analysts can move stocks or predict which will do well? Or how various ways of structuring compensation might impact retention in the event of a market correction or clinical trial delay? Lots of directors wonder these things as they prepare their companies to go public and try to figure out compensation strategies to help them attract and retain talent. So we tackle these topics, analyze data, build models, and share our findings.
- We're also investing in the next generation of our industry's leaders by teaching a course for current graduate students and recent grads working in industry using materials that we've created, some of which is available on our website.

Question: Does the Incubator impact the rest of your strategy?

- The incubator has definitely made us better shareholders for all our companies. What we are able to bring our newcos is broad and deep and serves companies well beyond the seed stage. Carnot can provide new assets, as well as the discovery and early development expertise. While our new companies are free to build internal discovery and early development capabilities, we find many of them find it more efficient to leverage the incubator rather than building in house. TechAtlas provides support for target prioritization as well as a large net for other assets and ideas. Our network of Venture Partners, EIRs, internal company creators, portfolio company executives, and board members provides the guidance and experience to not only create the companies but guide them through their growth.

- And the good news for many of our other company-forming peers is that all of this accrues to the benefit of any of our companies, whether we are the only shareholder of our own newco or, as is much more common, just one shareholder among many of a company someone else launched. We hope our peers will give us an early look at their newcos knowing that we'll bring our best game to the company-building effort.

Question: You sit on a number of private and public company boards. What would you say are the key differences in how VC investors vs public (or public/private) investors see the world and advise companies?

- So far, we've only taken board seats on private companies, and then in some cases stayed on the board as they went public. When we take a board seat on a private board, we're often the only ones with significant public markets experience and are expected to bring that perspective. But we also can tap into TechAtlas for strategy and indication selection, and we have a massive network, so we're often on the Nomination and Governance committees helping to recruit other board members.
- A key difference for us versus many other venture capitalists (though certainly not all) is that the IPO is not the beginning of the end for us. We play a very active role in both public and private companies. We've supported over 50 companies through their IPOs. We often look to continue to build our position into and after the IPO – after all, it takes a lot of work to find something great and we want to be able to continue to work with management to help grow the company long after IPO.
- So we'll often remain on the board after our companies go public, but unlike the board members affiliated with some traditional VCs, we're very much tuned into what would make us want to invest more in future financings. Other VCs may be constrained by their models not to invest more, and they tend not to have the public experience to know how the public markets will react to one scenario versus another and therefore when might be the best times for a company to prepare to finance. Again, I'm not saying this is the case for all other VCs—many of our VC peers have morphed into crossover investors and some will stay with their companies for a long time.
- I estimate that there are maybe a dozen investors with extensive public markets experience who regularly serve on the boards of their public biotech companies. There should be more, because young companies need that experienced perspective on the markets to help them make the best decisions. Public investors have never been shy about sharing their opinions and analyses with management teams, but while each thinks their suggestions are logical, we don't speak with one voice and don't get in a room to reconcile our conflicting ideas so that a company benefits from one or two well-thought out recommendations. Therefore, the collective assessment of the public markets as to the value of a particular program or

whether a company should partner tends to be heavily discounted in the boardroom, which is where conflicting ideas are hammered out into a single plan.

- So I think companies need at least one investor with extensive public experience on their board to help them openly debate the merits of those ideas and navigate their first few years as public companies. I think we'll see more such investors step up in the coming decade, but it requires that more funds accept the downside of being restricted from trading, and that's a big leap for some.

Question: How has the # of positions in your portfolio changed over time? What do you think is the 'efficient' number of positions to own in biopharma to maximize returns while minimizing risk?

- From the standpoint of risk and downside, it's our large positions that matter and we are indeed concentrated in a few large positions. Fewer than 10 companies typically make up more than half of our portfolio. But from the standpoint of upside, we are diversified across a broader set of companies that could move the needle for our fund. Simply because some companies are currently small, our large ownership stakes in them don't appear significant to some people. They may wonder whether we care about those positions, but what makes these investments important to our strategy is that we believe they have huge upside, so we definitely care.
- We have 1% positions that we expect to generate more upside than 4% positions. We would make the 1% positions larger, but for various reasons we can't (e.g. the company is too small, or the stock too illiquid at prices we find attractive). But those are positions that we might have the chance to increase in a future financing or if another large holder wants to unload blocks, so we pay all our companies close attention. For example, a few of the companies that I personally monitor closely represent less than 0.5% of our capital (the smallest less than 0.1%). In a few years, those companies might turn out to be large positions and major drivers for us.
- And even companies we don't yet own may be ones we want to add to our portfolio. So to some extent, every company that we might want to buy is like a currently 0% position we track in our portfolio. That may sound strange, but it's not strange to us.
- Fortunately, our team is large enough that we have the bandwidth to track a large number of companies.

Question: When platforms are evolving so quickly, how do you get comfortable that one you're investing in won't be displaced quickly by something better or different? A better gene therapy, gene edit, bispecific, mRNA, RNAi/ASO etc?

- We definitely think about that. Our TechAtlas maps articulate the competitive landscape of each disease area we track. We carefully track the companies and mechanisms we think are more likely to succeed and redefine the treatment paradigm 2, 3, and 5 years from now. And we certainly try to invest in the companies that will disrupt incumbents. Back during the HCV days, Vertex made sense until Pharmasset came along. Lev Pharma first developed Cinryze (twice-weekly IV infused drug for HAE) and was bought by ViroPharma and then by Shire, but then Dyax came along with a less frequently subQ injected drug that was better. Sometimes the incumbent makes the right acquisition and stays in the game, as Shire did by acquiring Dyax, and sometimes they don't, as happened to Vertex. We try to make sure that all of our companies understand everything that is publicly knowable about their competitive landscapes so that they can consider adapting, either by shifting their focus to other programs or acquiring emerging technology. We've also been approached by private companies that knew they could be a disruptive threat to one of our companies and liked the idea of us investing because we might then help bring our company to the table as a partner or even co-investor. When we're not sure who will win in a space but are pretty sure that someone will solve a problem, we will make several investments in that space. For example, back in 2013, we set out to find the world's next Alnylam. We funded both Dicerna and Arrowhead and urged them to pivot their efforts to GalNac conjugates.

Question: What's the best way for a company struggling with its valuation to get your attention?

- I know that there is a sense that a company can't break through to a large fund without an introduction. In our case, that's absolutely not true. Any company can email their non-confidential pitch deck to the contact information on our website, it will be circulated to the entire investment and research team, and if there is even a remote chance that it might be something we would invest in, someone will reach out to learn more.
- Some companies also have an antiquated notion that they must speak with a Portfolio Manager to have a chance at an investment. The inverse is true for us. Raj and I rely on colleagues with the bandwidth and expertise to conduct proper, deep diligence and frame the investment opportunity in the context of the entire competitive landscape, future financing requirements, and a valuation exercise so that we can decide whether we are supportive of an investment. If a company meets with Raj or me before talking to our better-informed colleagues, they are taking the long way through our process, because their next meeting will be their first real diligence meeting. The exception would be if it's an area that Raj or I know intimately, in which case we'll take that first meeting and pull in colleagues, but it's rare that either of us is our team's leading expert on anything.

- So we ask management teams to respectfully engage with whichever member of our team reaches out to them to learn more. Even the youngest-looking person on our team might be the smartest investment analyst you'll meet when it comes to your field because that person might have spent the last six months living and breathing everything to do with your field. That's the person you need to win over. Even if you come in through a more senior connection, we won't invest until that analyst gives a thumbs-up.
- If we won't invest, we'll probably tell you why and, for example, what data we would like to see before we would consider investing.

Question: So will you always tell a company why you won't be investing in them?

- Often we do. But I'll confess that sometimes we won't. In most cases when we pass on an investment opportunity, we aren't saying "no" but are really saying "not yet." We would like to have the chance to track the company in the future and possibly invest later. So when you tell a company that you won't invest, you hope they don't take it personally. And few do. Lots of good investors will also pass on any given deal, so we're typically in good company.
- But most investors will pass and not get deeply into their specific reasons for passing. They remain polite to the point of being evasive. And there is good reason for this. There is a real risk in sharing one's reasons for passing openly, since some management teams do take it very personally when you express concerns about a drug, data, valuation, etc. They hear criticism where an investor is really just trying to be helpful. In the past, we've been shut out by some management teams for being a bit too open with our reasons for passing. And we know that has happened to others. That's why investors often hold back.
- But we all know that no team can function well without everyone feeling secure enough to offer and receive constructive feedback. We believe our entire industry would function better if we all gave each other honest, well-intentioned, constructive feedback. Just as the person who punishes their colleagues for volunteering constructive feedback will rob themselves of that feedback and therefore only hurt themselves, companies similarly rob themselves of feedback when they cause investors to fear that they will be cut out of a future financing if they say the wrong thing. Passing politely spares everyone's feelings and preserves optionality for investors, but it's not the best outcome for everyone.
- Fortunately, there are many management teams who know this and proactively seek feedback with the reassurance that they will give us the opportunity to consider investing in a future financing. In those cases, we are forthcoming with our reasoning and in some cases have helped companies pivot to a plan we found compelling enough to invest in. Over the

years we've built many strong relationships with executives who come to us early in their financing process because they know we originate conviction (meaning that we don't need to know whether others are investing before deciding whether we want to do so), are deeply analytical, and, most importantly, if we aren't inclined to invest, will share our thesis and ideas for what the company might do differently.

- So when we don't invest, we would love to offer companies at least the benefit of our diligence. Some companies receive our financial capital as well as our intellectual capital, but all companies can at least get our intellectual capital, for what it's worth. And if the return to us for investing that intellectual capital is that the company wants to engage with us more closely and give us an earlier shot at winning a place in their next financing, then that's a great return. If more companies incentivized investors to share their intellectual capital, then more investors would do it, and that would make our sector even more efficient.

Question: Best thing you've done in 2019? One thing you regret most in 2019?

- My regrets are minor. I feel fortunate. I get to spend time with my family, enjoy what I do, and love the people I work with within our firm, in our companies, and among our peers. Raj and I are grateful that we've managed to survive as investors this far into our careers where we have so much to do with so many people we enjoy working with.
- We certainly have made investment mistakes. But we made most of these mistakes despite our best efforts, so there is nothing to regret as long as we learn from them. I only really regret the mistakes we repeat, and there are few of those these days.
- The best thing I've personally done in 2019 is finish writing a book, *The Great American Drug Deal*, which is based on the concept of the Biotech Social Contract that I've been writing about for the last few years. The book is coming out in January.

Question: What motivated you to write the book?

- For a while, I listened to the American public and our industry talking past another. Patients cried out that they couldn't afford their medicines and industry responses with explanations of how expensive and risky drug development is, as if that has anything to do with the patient. Congress was responding to patients by offering price controls and industry was responding to Congress as to why it shouldn't impose price controls (since we need to charge high prices to incentivize and fund expensive and risky innovation), but our own answer to the American public was tone deaf.
- Others proposed that there was a Biotech Social Contract that obligated companies not to take excessive price increases, and I realized that I too had always felt there was something of a Biotech Social Contract, but that it wasn't what others were suggesting. To me, the Biotech Social Contract is that our industry makes drugs that go generic without undue

delay (so that they accumulate over time as inexpensive generics that offer society great value) and society ensures that patients can afford the medicines that their physicians prescribe by through comprehensive health insurance without excessive out of pocket costs. But this contract was being stretched and torn by each side. Out of pocket costs were climbing and branded drugs were exploiting red tape monopolies.

- It's painful to hear how much the American public despises the drug industry when I see all the good that we do. I think, as an industry, we never made enough effort to connect with patients and just assumed that the public would appreciate our work on its own merits. But we never did enough to make drugs affordable for patients. For any given drug, our models always assumed less than 100% penetration into the eligible market due to our byzantine insurance system, but think about how cold that sounds. That's the root of the outrage and it was always there in our models. "*Incomplete market penetration*" means that a patient can't afford a drug and is suffering needlessly. Who do you think that patient and everyone who cares about that patient will hold accountable? Insurance companies made sure that patients blamed the drug companies. We're now waking up our mistakes. We should have done more to fight for complete market penetration, at least as far as affordability goes. The industry lobby groups certainly made their marks on the ACA, but it just wasn't enough.
- In response to questions about affordability, our response should always have been. "Patients can't afford drugs because their insurance plans don't want them to. That's heartless and outrageous and the system must be reformed. How can we help?" It's now clear that we should have all fought like hell for insurance reforms that would have required that insurance companies actually sell insurance that does what insurance is supposed to do: allow patients to afford what their physicians properly prescribe. That means capping out-of-pocket costs. Congress is considering such reforms but knows it will help the drug industry and wants something in return. They regard all drugs as if they were threatening to be expensive forever, and they want to impose direct price controls. I propose that those of us who care about incentivizing innovation offer a promise to America that all drugs will go generic without undue delay. Any company that has built a business model around extending the tail of their NPV model out as far as possible won't love that. But development-stage companies and their investors care about the front-end of the curve, the first 10-15 years of the NPV model. So there's a growing tension and potentially a rift between the innovators and the tail-extenders, and it's important to the sustainability of our industry that the innovators prevail. While price controls on the front end undermine the incentives to fund development-stage research, having drugs go generic after the first 10-15 years of patent protection does not (since those outer years are heavily discounted in our models when we are considering whether to fund development). There are some caveats I get into in the book.
- We are all at our best when we're hustling to discover something new. But as we develop more gene therapies and other complex biologics that can't go generic, we risk becoming

addicted to indefinitely collecting rents. And when a company has the security of milking an ungenericizable old drug, it loses some of the hunger that would otherwise drive it to invent or acquire new assets. That's no good for society. Patent cliffs keep everyone motivated, and that's how it should be.

- So I hope this book helps our industry make a case for the work it does and moves Congress to make drugs affordable to patients by reducing out-of-pocket costs rather than imposing price controls on drugs at launch. In turn, to ensure the sustainability and vibrancy of our industry, the book makes the case that we need to support legislation that ensure that all drugs will go generic without undue delay.

Question: Have you shared the book with anyone yet? What's been the reception?

- We teach a course at RA Capital for graduate students and recent graduates working in biotech and I've given them earlier drafts of the manuscript. One student summed it up perfectly by saying something along the lines of "I used to be conflicted about going into biotech because of how evil everyone makes the industry out to be, but now I'm proud of what I want to do. And I know how I'm going to respond to my grandma when she rips into me about patients not being able to afford insulin."

Thank you Peter! Appreciate your thoughtful insights. Stay tuned for more from our PM Corner series...ideas for topics and contributors are always welcome!

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Coverage Universe			Investment Banking Services I Past 12 Months		
Ratings	Count	Pct.	Ratings	Count	Pct.
Buy	418	52	Buy	97	23
Hold	323	40	Hold	37	11
Sell	40	5	Sell	3	8
Coverage Suspended	16	2	Coverage Suspended	8	50
Rating Suspended	14	2	Rating Suspended	4	29

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