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BIOTECH'S NEW ERA: INNOVATION AND COMMERCIALIZATION

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Biotech's New Era: Innovation and Commercialization

Stephanie Sirota: It started with a science race 13 years in the making. Mapping the majority of the human genome with two entities—the U.S. government-backed Human Genome Project and the privately funded Celera Genomics—announcing their rough draft of their findings in the year 2000.

And like ripples in a pond, this major milestone would mark the beginning of a tidal wave of innovation. In the decade that followed, scientists identified the root cause of genetic diseases and tested bold new therapies in the lab with new tools to boot.

Academic science built new modalities, and they were off to the races. Following that, academia passed the baton to industry, and we saw firsthand how innovation was becoming a reality.

And while looking back and taking stock of where we are is important, it's also important to look ahead as we enter the next era of transformative innovation. And that's why I'm so excited to welcome a true innovator, a visionary, my partner and friend, our own Rod Wong, Managing Partner, Chief Investment Officer, and founder of RTW Investments.

I'm your host, Stephanie Sirota, Chief Business Officer, and Partner at RTW. Today, we're taking you through the evolution of the biotech investment space, and we're going to share with you some of the bold predictions about where the industry is going and why investors should take note. Rod, thanks so much for joining us on the podcast today.

Rod Wong: Good to be here.

Gene therapy and biotech

Stephanie Sirota: It's amazing to see how much biotech has evolved over the last two decades. Let's take our listeners through that innovation life cycle and point out the most important takeaways in the last 20 years. You were in med school at Penn when the first genome was sequenced. Can you take us back to that first milestone and tell us why it was so monumental for biotech?

Rod Wong: I think it was '99 or 2000 that the first sequence was completed. The government, the Human Genome Project, did it for about $3 billion, and then Celera, the private company, got it done for about $300 million. It took about 15 years before the cost per genome sequence dropped below $1,000.

And that's when the downstream benefits of having that information really started to accelerate. So, why was it so transformational?

It's roughly estimated that about two-thirds of human disease has some kind of genetic contribution to it. So, the majority of disease. There's around 10,000 rare diseases in the U.S.

I think if you add them all up together, it's about 10% of the U.S. population. Of those, 80% have some kind of genetic contribution, and another 80% of that I believe is monogenic, or caused by a single gene. So, somewhere north of 5,000 rare diseases are caused by a single genetic mutation.

Having that genome sequence basically opens up the understanding of so many of the drivers of human disease and provides innovators with the targets to go after, so that then you can develop drugs or cures for those diseases. So, it was a hugely enabling step for innovation and one of the major contributors to the boom that we're seeing.

Stephanie Sirota: During that time, one of the first gene therapy patients was treated and sadly passed away. We had this juxtaposition of the greatest potential unlocking of genetic information against brand new technologies in their infancy, years away from primetime.

Rod Wong: The very first gene therapy patient was treated by the NIH in 1990. And it was a patient with a very rare immunodeficiency disease called ADA-SCID. But when I was at Penn in '99, there was a patient named Jesse Gelsinger with another rare disease called OTC deficiency that had a tragic outcome.

Jesse was treated with an adenovector. Obviously, this wasn't known prior to getting treated, but he ended up having what's called a cytokine storm: a really massive immune response that led to multi-organ failure, and then tragically him passing away.

That was a major moment in gene therapy. In general, the field slowed down, before re-accelerating on the back of some improvements to the types of viral vectors that were used a few years later. With gene therapy, it's taken time. It's still trying to figure out some of those challenges. Not every technology at the beginning is ready for primetime.

Stephanie Sirota: You're heavily influenced by this renaissance that was happening in the biotech space: the new development, the new access, and tools. After med school, you went into investing. So, your first portfolio manager job was in 2005, and then you founded RTW in 2009. How would you characterize what made you a successful investor during that first decade? Let's say '05 to 2015.

Rod Wong's journey into biotech

Rod Wong: Biotech honestly was a pretty small industry at the time. I think the total publicly traded market cap was around $300 billion.

80% of that was in the U.S. And half of that market cap was four big biotech companies: Genentech, Amgen, Gilead, and Biogen. The way I'd characterize the industry at the time was there was relatively low innovation, especially when you compare it to what we're living in today.

As a result, there are relatively few specialist firms doing what we do now. I remember a big fund at the time when I started was $0.5 billion. I interviewed at a couple of hedge funds around that size. I thought it was the hugest thing that you could possibly imagine.

And if I remember right, the top couple largest firms were maybe just over $1 billion to $2 billion. The talent situation I would describe as: you had an edge if you had any kind of generalist scientific background.

That was enough to have an advantage, as a healthcare investor. You honestly didn't even need any financial skills at all. And if you had basic finance or forecasting ability, that was also a major advantage.

Me personally, fresh grad, scientific background, had an MBA, working with a small team—that was enough to have major edge in predicting whether science was going to work or whether a market was going to be interesting or not in terms of the size of the business opportunity.

Stephanie Sirota: You lived through the GFC, and capital was scarce. But you had this huge belief in biotech. How'd you know where to put your money and where to focus your attention?

Rod Wong: We tried to comprehensively follow the innovation. And we tried to assess where the odds of success would be higher than average. And a couple of those areas were rare disease and RNA.

And those were the places that had the combination of higher odds of success as well as there was a business there that you could underwrite, that was sizable enough.

It was what I was interested in. It was what I was educated for. And honestly, I just really love the job. Anyone who is picking the ideal industry probably wouldn't have picked biotech to sub-specialize as an investor. It just wasn't a big enough field then. You had to do it because you enjoyed it. Early in my career, the things that I did have an advantage in so far outweighed the rest that it allowed for us to have some success.

Stephanie Sirota: Do you attribute your knowledge of the fundamental science to keeping your footing, even when the markets were wild? During the global financial crisis, the 2015-'16 period, Valiant came crashing down, Theranos was exposed as a fraud, and Hillary's famous tweets on drug pricing really rocked the sector. Nobody wanted biotech.

"When you've been in this business for as long as I have, you have known pain."

Rod Wong: The financial crisis was not long after I was in the business. We know what humble times look like. The decade from 2015 to now, that was a super interesting time. Because in contrast to when I started, innovation was starting to accelerate.

You had this bull market for a period where you saw an explosion of new modalities, right? We only mentioned one of them so far, which is RNA. But there are about a half dozen others—many of which we talk about all the time—like gene therapy, cell therapy, protein degraders, ADCs, radiotherapy. All these modalities kind of hit the scene during that time. That transitioned to a bear market. Both the tail of the boom and the bear market were amplified by a couple things.

One was COVID-19. And then also the crash because of the reversal. It was also amplified by drug policy. The second half of that decade you had a very high amount of policy uncertainty and actual change.

You had the passage of the IRA. I think anyone who's been doing this business a long time needs to be used to it, needs to know how to navigate those kinds of things top down. I think there are investors that always see opportunity in bear markets—if they have a fundamental value framework, for example.

And that's our investment style as well.

So as terrifying and challenging as bear markets are, they're also the time where I see some of the most opportunity.

And so that's a reason to be excited and a reason to stay really interested in the job.

Stephanie Sirota: Well, you clearly did, because during that bear market is when you doubled down and reinvested in the firm and took the firm through a major growth spurt. Not just head count, but you grew AUM.

You invested across important subsector specialization, but also new functional areas. I'm curious: do you see yourself now as a business builder or an investor? Clearly both. But where does that line blur?

Rod Wong: Investor or Business Builder?

Rod Wong: I've always thought of myself first and foremost as an investor. I had to become a business builder to do what we did. Our growth was significant.

And during that period for part of it I had to be a very hands-on manager. Now, I'm very happy that that period of my career is past.

And I've been able to refocus not just as an investor, but then retain the parts of the business builder that I actually enjoy and think I have some talent for, which is the strategy piece.

I'm trying to focus on just hanging onto strategy and pushing as much management to professionals as possible.

Stephanie Sirota: That first decade was the decade of discovery, followed by the next decade—this decade of development. Tell us what's next.

Rod Wong: We are at a super interesting inflection point: the direct progression from the boom in early-stage science.

Some of that science matured successfully, and the result is you're getting more new drugs across the finish line than ever. And businesses that emerge from those successful products.

This next decade will not be the decade of early-stage science, but will be the decade of commercialization and successful businesses being born from that science.

That is a super exciting phase: to have as many transformative medicines as possible to make a dent in human disease. Exciting early-stage science is simply a stepping stone to that end goal.

Stephanie Sirota: Many investors still think about biotech as this pre-revenue, high-risk science project. Now you're saying that they should really reframe their understanding of the sector today. The top and largest biotech companies —Amgen, and Gilead, and Biogen, and Genentech—have you seen new entrants in that space?

Rod Wong: The total industry cap now is a little shy of $1.5 trillion. So, it's up about 4x to 5x. Also, the concentration is less. It's about twice as many names now that make up half of the market cap.

"You're seeing the leadership of the sector broaden out. I think that's going to continue. The industry is going to grow even faster over the next decade, and that leadership is going to be even broader."

When we have conversations with our investors, we like to bring up this one example, which is that the brand names in biotech, that list has been relatively static for 20-plus years.

But for the first time, that list is changing, and many people are still not aware of companies like Argenx, or Alnylam, or Insmed, or BeOne. All of those companies have now larger market caps than Biogen, which was one of the Big Four when I started in the business. I think that trend is only going to continue and probably accelerate.

Growing trends in biotechnology

Stephanie Sirota: With the convergence of technology and AI, do you think investors that once focused on tech will see the potential on the scientific tech?

Rod Wong: Our friends in tech bring a different lens to our sector. Some folks are getting excited about our sector again, about the potential that AI has on drug discovery specifically.

It's going to be the most significant thing to impact research productivity in our space since the genome. And maybe the impact will end up being even bigger.

Our industry spends the highest proportion of revenue on R&D of any industry, I think. It's roughly 25% for the large cap companies.

I believe the next highest are chip companies, software companies that spend a little bit more than half of that percent of revenues on R&D. But bottom line is, our industry spends an enormous amount, because R&D in our space has been historically a really difficult, low return exercise.

The failure rate is 90%. It historically took over a dozen years from the beginning to the end of the process. If AI can increase productivity in terms of odds, timelines, and quality of the product that you get out the other end, you think about the big picture impact that could have on an industry that spends 25% of revenues on R&D.

If productivity is increased, you get more revenue for that 25%, so the growth increases.

The other possibility is you don't have to spend 25% on your revenue to get the same business result, and then maybe you look a little bit more like some of these other industries. More efficient use or output out of R&D. And if that happens, I think perception of our industry could change a lot.

Stephanie Sirota: It sounds like we're sitting on a volcano of potential from a valuation perspective, but also a next wave of value creation from great new drugs. Where do you see that next wave coming from?

Rod Wong: These modalities that we talked about, many of them are maturing. They're all different in terms of how broad their applicability is, how much new product ultimately that they can produce. Holistically as a group, you're going to see record-setting numbers of new products, and then the promising businesses from that, five, ten years down the line.

Stephanie Sirota: Sometimes people say, "I've gotten burned in biotech, and I don't want to touch it again." It is a sector that can be very cyclical. Maybe tell us a little bit about your views on risk management and conviction when sentiment turns against the sector. Because that's what we've been living with for the last few years, and now it's starting to turn in the right direction.

Generating Alpha in Biotech

“The number one thing you can do in terms of risk management is to generate alpha. This is a space that remains highly inefficient.”

Rod Wong: If you can generate consistent alpha, that is your best margin of safety in down times for the market or the sector. You want to pick investments with a favorable up-down or risk/reward.

So even if you transition from a bull market to a bear market, you get some margin of safety from being disciplined in terms of your valuation framework.

And you get conviction as well, when your investments move against you, that you won't make portfolio management or trading mistakes.

We have one fund where we have the flexibility to adjust our gross and our net exposure, especially our net exposure.

Generally speaking, in periods of high valuation, we can reduce that net exposure to the market and reduce our losses if the market was to transition from one stage of the cycle to another.

Stephanie Sirota: Generating alpha is the basic principle of what we're designed to do as an investment firm. The prevailing wisdom has always been: invest in the science, and then sell the launch.

But your rebuttal to that is we're entering this new era of commercialization. Maybe talk to us about some of the other areas—that here at RTW we like to refer to as alphastacking—where you've been able to gain edge as an investor, outside of science, which is obviously fundamental.

Rod Wong: If you look at a lot of what made investors in our space successful over the last decade or so, it’s the ability to underwrite early-stage science. That's always going to be valuable. Being comfortable and knowing what you're doing when companies are at commercial stage is going to be an increasingly valuable skill set.

For us, for example, we're talking about portfolio construction. Today, a majority of our investments are in commercial stage companies. Having deep expertise in commercial forecasting of those kinds of businesses is critical right now and I think it’s going to be a huge driver of who succeeds in the next decade.

This term, alphastacking. Big picture: find as many potential sources of alpha as possible.

You want to test them, right? And then if it looks like a real source of alpha, you want to maximize that advantage. And we take that intentional approach to everything that we do. The two biggest buckets: underwriting science, underwriting commercial—there's other things that are very complementary to that.

We had the foresight to stand up a Government Affairs function when Trump won the election. And it's been incredibly valuable to help us navigate that policy uncertainty. That's not something you would think of as a key source of alpha in most environments. Because of the way we're organized, and the way we think about alpha, we could jump on it when we saw the opportunity and then capitalize on it.

Stephanie Sirota: That's great.

Rod Wong: Maybe before we wrap up—let's flip the script a little bit. I know you've been fielding a lot of questions about a couple topics: longevity and preventative medicine have become buzzwords that we hear about a lot, especially from our friends in tech. What do you think is real? What's hype?

Stephanie Sirota: People like the concept of longevity, preventative medicines, thinking about real impact to one's health span outside of lifespan. But buzzwords are not businesses. That's not treating disease, which is what our business today is designed to do, to really interrogate science and then evaluate how big some of these opportunities are.

For longevity, the biggest gift that society was just given and now at a reduced rate for non-insured patients is the GLPs.

So, Lilly going direct to consumer, and Novo—all of those new drugs for weight loss have a tremendous impact that is going to help a lot of people live longer and be healthier while they are alive.

On the preventative medicine side, there's not a lot of medical school that's really focused on how to live healthier: things like nutrition, sleep, or fitness.

They're certainly important, and people should absolutely educate themselves, and adopt the healthiest practices.

But for right now, they're lifestyles, and they're not real businesses that are investable from our perspective.

Rod Wong: Along those same lines, what about these adjacencies to healthcare?

Trends like wearables, biomarkers that give people the ability to monitor their own wellness, and in some cases, manage their chronic diseases?

Stephanie Sirota: So many conversations that I have outside of the business setting are on health, tech, and consumer.

And that convergence is upon us. I think we're just beginning. I'm actually really excited about the opportunities that are emerging in that space.

I said that preventative medicine is not a business. But maybe it's not a business yet. The opportunity is not fully crystallized, but it's coming.

Rod Wong: Totally agree. And we are following some businesses like that right now in our medtech practice.

Stephanie Sirota: That's right. With the AI impact, I think there's going to be a lot more to say when people start tracking their own metrics.

Rod Wong: And then maybe shifting gears, what's new in terms of the investor allocator landscape?

What kind of people are you talking to right now? Where's interest in our sector coming from?

Stephanie Sirota: It's so exciting. This is going to be a whole new chapter in capital that can come into this sector, and fund tomorrow's innovation.

And that's coming from private wealth, private bank clients, high net worth investors, and retail. I think this also is part of the convergence trade.

Because as people hear more about how important this opportunity is, how impactful biotech, health, and biopharma are on society and in our portfolios, I think people are getting a lot wiser to that.

We're having a lot of conversations with private bankers, with financial advisors, and expect a lot of private wealth money to come into the space.

Okay, so with all that talk, if you want to look ahead ten years, what headline would you like to read about biotech, or RTW, in 2035?

Looking forward for RTW

Rod Wong: If the headlines are the number of novel new medicines reaching patients every year is double each year from what it is today, if the efficiency of drug discovery has improved dramatically thanks to everything we've talked about—including AI—so that these businesses become more predictable, higher growth businesses, I think that would be great for the industry. It'd be great for health.

"For RTW, our goal is to work with the most promising entrepreneurs and companies with the most promising drugs in development and on the market, and help them on their journey."

Of course, by providing capital, but also, we do it in other ways too. I would love it if we play a role in broadening understanding and interest in our space.

I actually have a new book out that covers a lot of the issues we've been talking about. It's actually a healthcare policy book focused on innovation.

For people who are interested, they can actually go to the website and find out how to get it.

Stephanie Sirota: Innovation is the Best Medicine.

Rod Wong: That's the title.

Stephanie Sirota: This is going to be an essential read for anyone that wants to learn more about biotech.

I would like to just add one thing to what I would also like to read about in ten years for the sector, but also RTW. I say this coming from my career as an investment banker and getting a Master's in journalism. There are a lot of avenues, and there are a lot of ways to have a role in this sector, and in our business too.

Because we need storytellers. We need capital raisers. We need dealmakers. We need strategic thinkers. We need people with legal backgrounds. There is a lot more than the primary science piece. So, the industry is open for business, and it's really welcoming to a lot of smart people to join us.

Rod, thank you so much for joining us today and sharing your insight on biotech's next frontier.

Rod Wong: Thanks a lot. It was fun.

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