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**Speaker 1:** The *BioWorld Insider Podcast*.

**Lynn:** This is the *BioWorld Insider Podcast*. I'm Lynn Yoffee, BioWorld's publisher. It's tough out there for biopharma companies looking for partners right now. Despite strong deal activity over the last two years, the volume and value of partnerships began sliding in the first quarter of '23. Mergers and acquisitions are down too, compared to prior years, but are better times ahead? Today, BioWorlds staff writer Lee Landenberger is talking with Karen Carey, our managing editor and senior data analyst. She just wrote about biopharma deals in the first quarter and completed M&As. Welcome, Karen.

**Karen:** Hi, Lynn. Good to be here.

**Lynn:** Also with us is Tim Shannon, a general partner at Canaan Partners. Tim started his career as a physician and later became the CEO of publicly traded CuraGen, an oncology firm. He's been with Canaan since 2009. The newest fund from Canaan has $850 million in new capital, including an over-subscribed $650 million fund for seed and series A financings. Tim told us ahead of this episode that he's somewhat cautious, but sees better times ahead for the market. Welcome, Tim.

**Tim:** Thanks, Lynn. Happy to be here.

**Lynn:** Over to you, Lee.

**Lee:** Thanks, Lynn. It's great to have everyone here. You all are uniquely knowledgeable about the current market, which had its troubles, but we have some new numbers in. We have a better idea of where things stand. Karen, you wrote a big story for Bioworld earlier this week, it was April 18, you wrote about the first quarter's deals and the M&As. With your reporting, what was the big takeaway?

**Karen:** I guess the big takeaway is that while deals are down from last year, they still have a respectable showing so far in 2023. While M&As are somewhat depressed, we see signs of recovery with some of the large ones pending. Financings, on the other hand, they're quite a bit down from recent years. I guess companies are accessing capital through partnerships, and of course, M&A is a good option for pharmas trying to build their pipelines.

**Lee:** With these numbers in, can you tell me how they compare with the first quarter of last year?

**Karen:** Okay, let's look at financings. When we track financings we're tracking everything from IPOs and follow-on offerings to private placements and venture capital amounts. From those four types of financings, in the first quarter, the biopharma industry raised $15.6 billion according to our data. Now, there were 276 transactions that we counted. If we look at the value of those financings, the $15.6 billion, we are ahead of last year's first quarter by 14%. Last year, the figure was about $13.7 billion, so almost $2 billion less, and it was the lowest amount raised for a first quarter since 2017.

Now, Q1 of 2023 is the second lowest amount raised since 2017, so we're doing better than we were last year, but not as well as some other recent years. I also wanted to say that the lower financings could be happening for a few different reasons. Of course, as you know, there was a frenzy of financings in 2020 and 2021 during the pandemic. BioWorld tracked well over 1,000 therapeutics and vaccines and development for COVID. There was huge government support, excitement over what the industry could achieve.

Generalist investors jumped in, and that resulted in 2021. That first quarter $38.3 billion was raised, so more than double of what we've seen this year.

In 2022, generalist investors disappeared. There were concerns over inflation, the Ukraine-Russia war, drug pricing pressures, the World Trade Organization's intellectual property waiver, and of course, Inflation Reduction Act. All of this made it harder for companies to access the public markets. There was also the high cost of capital to consider.

**Lee:** In that April 18 story, you wrote that the volume and the value of partnerships began sliding in the first quarter of 2023. Can you give me an idea of what the numbers look and what were the largest deals?

**Karen:** Sure. We track deals as licensings, collaborations, and joint ventures, and then we track M&A separately. Four deals. We had 357 of them for the biopharma industry in the first quarter of 2023. All of those combined, they were worth $48.1 billion. That's a 16% drop over what we saw in the first quarter of 2022. The volume also is down by 24%, but when looking at all first quarters back to 2017, 2022 was the top Q1 for partnerships. 2021 had the highest volume, but 2022 had the highest value, $57.5 billion.

Even though we're behind last year, the values of partnerships in the first quarter of this year are the second highest in that same timeframe. We did have some pretty big deals in Q1. We had Bristol Myers Squibb and Evotec. They signed one for neurodegenerative disease therapies for about $4 billion. We had AbbVie and Immuno join together on oncology antibody targets for $2.8 billion. We had MacroGenics and Synaffix expanded an antibody-drug conjugate deal with another $2.2 billion.

Those three joined with about 12 other deals in Q1 to become 15 mega deals. We call these mega deals, those that are worth $1 billion or more. Those 15 mega deals are about 56% of the overall deal value in Q1.

**Lee:** Did those deals focus, was there a trend in the therapeutic area or modalities among those deals?

**Karen:** As we've seen in the past, a good chunk of them are for cancer. 32% of these partnerships were focused on cancer, 17% for neurological disease. About half are those two therapeutic areas. As for modalities, small molecules represented 35%. Cell or gene therapies were 13%. Monoclonal antibodies were 10% of those deals.

**Lee:** I want to ask you about M&As. They continue to struggle. Why so much this quarter?

**Karen:** M&As, they've not been doing well the last few years. Our numbers show there were 34 in the first quarter that closed, and they are valued at about $9 billion. Now, when we do this, we're only counting the ones that close. Compared to last year's first quarter, we did have more close this year, 34 versus 25, but the value of those M&A were significantly down $9 billion versus $16 billion.

In comparison to other years, M&A are struggling, but we did have three M&A in Q1 that were worth more than $1 billion. That was AstraZeneca acquiring CinCor Pharma for $1.8 billion, Sumitomo acquiring Myovant for $1.7 billion, and Merck acquiring Imago BioSciences for $1.1 billion.

They may have been struggling the last few years because companies were able to raise money more easily or maybe there's fewer M&A because of a disconnect. I've heard it said a disconnect on valuations between buyers and sellers. We do think there may be a rebound that's happening, and that has to do with some big M&As that are pending in March. Announced in March was Pfizer's offer for Seagen for $43 billion. That's expected to close later this year or early in 2024. We also have Amgen's $27.8 billion offer to buy Horizon Therapeutics. That was announced last December. It's expected to close mid-year.

Merck is buying Prometheus for $10.8 billion. That was just announced a few days ago and could close as early as the third quarter this year.

Also this week, I think you wrote the story, Lee. We had GSK offering to buy BELLUS Health for $2 billion. If all of those close this year, we'll be ahead of last year. I will say those first three I mentioned, Pfizer-Seagen, Amgen-Horizon, Merck-Prometheus, if those close, they're going to be on BioWorld's top 20 list of acquisitions of biotech developers, so there are some big ones.

**Lee:** Now that you've done this first quarter story, do you have some ideas, some of the trends that point toward the future?

**Karen:** It's always hard to say when you talk about the future. I guess just listening to some others speak and reading and seeing what other analysts are saying, I hear quite a lot about how crowded things have become, how many scientists are out there trying to raise money. Ultimately, what is supposed to happen is the best science should get through. They should get the funding, the partnerships, et cetera, but I do suspect these crowds will also result in some very good opportunities becoming invisible.

Hopefully, as we move toward the future, our industry will get better at messaging so that there's a better understanding of the industry and how it works, because there has been a lot of resistance that we faced from Inflation Reduction Act, drug pricing, WTO waiver. Again, these things are making it harder to drive innovation forward.

**Lee:** Thanks, Karen. Some of those are concerns of Tim's too, so I want to turn to him. Tim Shannon from Canaan Partners, he's had a long career in health care and he's a long-term investor with a big-picture view. It's based on years of experience. Tim, I want to ask you, is there anything that jumped out at you from that Q1 data, whether it was good or bad?

**Tim:** Yes. I would say there's still a lot of uncertainty in the direction of the biotech market in general. I think that uncertainty is obviously greater with the smaller companies who are pre-revenue or just with their early revenues compared to the larger companies who have revenue streams. I think both of them are facing uncertainties from a whole range of directions some of which Karen mentioned. I think when there's uncertainty, again, people, are generally more cautious and more considerate of what they're doing, whether it's M&A or partnerships or invest in a new company.

I still think a lot of uncertainty, which raises questions in minds and people and companies and investors and keeps things at a slower pace than in times when there's more certainty, be it on the geopolitical level, the US political level, the macroeconomic level. Again, you can throw a whole host of other things that are creating this time of uncertainty. I think until some of that plays out a little bit, my guess is we're going to bobble around at about this level.

**Lee:** Well, you described yourself when you and I talked about two weeks ago as being extremely cautious, but you're in the fray. I want to know, what were your biggest concerns in putting together this latest fund?

**Tim:** Well, again, I think Canaan has had good fortune to be in the business for over 35 years now. We have excellent LP relationships and a track record. Again, I think what helped us is we have a track record through the ups and downs. In times like this when frankly, a lot of LPs are cautious I think because of the history we have of navigating these waters, we were able to raise money.

As I think about the environment, I think as we discussed, I personally was a little bit on the sidelines, I would say, in 2021, '22, just because I thought particularly 2021, there's just so much money flowing into the system, and valuations were so high that it was hard for me to get my head around a realistic investment thesis and making an investment.

I think those issues have started to work their way out of the system, meaning valuation expectations as well as fundraising expectations, are starting to resettle a different place, which I think makes investing more interesting again, from a return profile perspective.

Just recently, a company was announced, they did a series A company called **[unintelligible 00:14:14]**. We actually closed that last year. That was something I was working on last year.

I have a couple more in the hopper that have been working on for the past six months. I do think from a private perspective, again, there's been a recalibration of valuation that does make it a much more interesting time to invest again, with the belief that by the time those investments come to fruition in those operating companies, the markets will have gotten to a better place so that that value can be recognized in a market that's more receptive to value recognition than today's markets.

**Lee:** A big picture on the markets or the headwinds that we discussed a couple of weeks ago, politics and regulations. Especially for small molecule oncology, can you give me an idea of what your biggest concerns are with that?

**Tim:** There's a range of them that Karen mentioned, and I'll just mention two before I get into this. One, I think, is the patent issues that came up during COVID and continue to persist in terms of respecting patents worldwide certainly was a big one. The other one I would just mention on the side on the M&A issue is, again, we have a very aggressive FTC intervening in what they believe is trying to protect consumers via anti-competitive mergers. It's all in the eye of the beholder, but that is definitely on everyone's mind when they consider M&A.

M&A it's in big companies, but it's also M&A with big companies and small companies. Those are just two things inside.

With small molecules and oncology, I think in oncology in general, there've been a number of issues. First of all, I'd like to say we've had an incredible 20 years in oncology drug development, which has resulted in a tremendous amount of investment going into that area. Part and parcel of that has been part of the reason we've seen a reduction in cancer morbidity and mortality in the world and in particular in the US. It's been an incredibly productive time enabled by a couple things. I'll give this backdrop first and I'll go with my concerns.

One is the underlying science. Cancer was a huge beneficiary of the Human Genome Project and the advances in sequencing and making sequencing available cheaply and in real time. As you know, cancer is in-part been dissected into a number of genes that mutate during life and cause cancer. That's really given us leverage to develop very effective drugs that impact people's lives in great ways. Also, provide a lot of reward in terms of the investment and the revenue side of that. That's been a big driver.

The other big driver, though, has been two things that are-- so that hasn't changed. That won't change. That will remain put. Two positive features that are now tipping the other way, I would say, has been the incredible regulatory support for oncology drug development, number one, and then the pricing support in the marketplace for pharmaceuticals in general, in particular oncology drugs, which really have come on the market in the big time in the last 20 years.

Again, on the-- I'll start with the pricing side so that the biggest risk there is, is the Inflation Reduction Act, which targets small molecules and effectively limits your patent protection. That's just the only way to say it. It takes your normal patent protection and takes it down to nine years when, frankly, while there's this negotiation process, it's unclear how much of a negotiation that's going to be versus just the government setting the price.

While that just affects Medicare, it will affect the entire market because once those prices are reset for a drug in Medicare, private insurers are not going to pay 30% or 40% more for that drug. It will move the whole market.

Moreover, it's not a onesie-twosie sort of thing or whatever the first number of drugs is eight or 10 in the first year. If you pick a category leader, for instance, in lung cancer and you reduce its price by 30%, everything in that category will have to be reduced comparably relative to that market leader. Again, it really has a profound impact of shortening the commercial life of small-molecule cancer drugs.

That's an issue in general. For cancer, it's a bigger issue because cancer drug development, the first approvals are in the most desperate patients. Those are people who have metastatic disease, have gone through all available therapies and get benefit from this new therapy, and it goes on the market.

Those aren't the most important markets, though. Cancer drug development over time progresses from those worst-case patients to patients you can potentially cure. Patients who have their first metastatic disease and have an opportunity to cure or, an example of where you would go four or five years after that first approval. After those metastatic patients, you would go into patients who've had their tumors resected but have a high chance of recurring with metastatic tumors with your drug. That's called adjuvant therapy or neoadjuvant therapy.

That might come on the market four or five years after that because those are much longer studies, much larger investments, and there's a de-risking element by showing you have activity in the worst patients. By doing that, you know you're more likely to have activity in the patients who have less disease.

Cancer drug development goes through a time-oriented sequence where you go from smaller markets to larger markets over time, and that spreads out the investment horizon. Also, as I said, de-risked it because if it doesn't work in the advanced populations, you're probably not going to spend the money in those populations. That takes decades to do.

Now, theoretically, you have nine years. That really upends what has been the normal cancer drug development. What it probably will do is compress the timeframe in which you need to make all those investments and make them more risky again, because you won't be de-risking them by doing them sequentially. Now, and I work here, I should work here, I work there, I should work in the next one.

I think in long and short, that you have two things going on, one on the pricing side. One, you're constraining the backend, so you're diminishing revenues. Two, you're increasing the cost and risk of development, and that's just the bad thing for investment. That's really the opposite of what you want to do. That's on the pricing side.

Then just a briefly on the regulatory side, as you're all aware, there's been a huge pushback on accelerated approvals. Again, this era was heralded by drugs like Gleevac and Velcade that got approved in single-arm uncontrolled studies based on response rate and duration of response. These drugs' initial approvals were literally in 50 to 100 patients where 25% to 50% of them showed a great response uncontrolled and they were approved.

Those days are gone. There's been pushback and accelerated approval. What accelerated approval has basically become now are large randomized controlled studies, and your acceleration is getting approved on progression-free survival with overall survival still to come in the same study. The pushback and modulations and accelerated approval have resulted in a change from really small, efficient studies to get those first approvals to much larger, much longer, much more costly approvals to get the accelerated approval based on PFS. Frankly, OS, overall survival's usually in the same study and it just will take a couple years later.

That was regulatory tailwinds that really propelled oncology to be so attractive from an investment also have taken a negative turn. I think it is about both the government pricing issues, which are negative, and then FDA buckling down on accelerated approvals.

Now, I would just say there are two sides to this. I think everyone would less costly drugs, and I'll raise my hand there. I agree. I think I understand the reasons behind trying to do this. For some parts of society, this might be the best way to do it, but I am fearful that these create negative headwinds in a field that has been revolutionary in the last 20 years. I think you'll start seeing some investment tipping away from oncology and out into other areas. I know that's… happy to take any follow-ups.

**Lee:** No, that's fine. I think that's great. I wanted to ask you about that while we were talking about costs and pricing. You had mentioned that the US pricing subsidizes medicines for the rest of the world. [chuckles] It just seems like it's what comes with the territory, but I wonder is there another way to do this?

**Tim:** I don't know what-- I think it's true. If you look at the profitability of drugs elsewhere in the world, if we didn't have the United States there wouldn't be an industry. There wouldn't be an investment in the industry. I think that's just a fact. It's a very difficult issue to deal with, so obviously our government cannot do anything to force other governments to price their drugs differently. That's nearly impossible.

Companies tend to make them available, again because they feel some obligation to do so in countries where they can at least break even. Again, I would say I think there are more rational ways to reduce cost than what I would call blunt instruments, which are going to impact investment. Again, I'd like to find ways to reduce fuss in ways to actually encourage investment. I think that there are ways to conceive of that doing, but again, they're difficult to do.

At the end of the day I think this is the way I look at it, the US subsidizes a lot of things in the world. The one I always think of is the defense of the free world. We are the world's military and we invest in the military in the US knowing that. We know that the world depends on us and we are willing to step up because it's in our best interest as a company. To me, that's the cost of leadership and leadership in the free world.

I think there's the same cost to the leadership in science and medicine. There should be an expectation if we are going to be a leader, that we are going to foot more of the bill. As I would say, what's the alternative? If we don't do that, who is going to do it? I don't know the answer to that. I think it's likely to be no one, or it's going to be someone that actually we don't want being the leader in doing that. Again, I just don't think that's the world we want.

I think the expectation that prices in the US should be the same as prices in the other world are just that they're just not consistent with US leadership in science and medicine.

**Lee:** Is there a big feeling that they should be that consistent? I wasn't aware of that.

**Tim:** Well, I think every time, when you hear all the pushback on US prices, the common example people will use is comparative pricing in other countries. I see this in pieces all the time that write about the distortions in US pricing. It always goes to, how can it cost so much in the US when it's 50% of that in Germany or 30% of that in Europe? I think it is a frequent argument that people are critical of US pricing use. I see it all the time, but I think, again, there are reasons for it.

**Lee:** Well, Tim, thank you very much for sharing your expertise. Best of luck with the fund. We'll be watching it.

**Tim:** Thank you.

**Lee:** Karen, also thank you to you. I look forward to seeing the second quarter numbers.

**Karen:** Thanks, Lee.

**Lee:** Oh, you're welcome. Glad to have you. Lynn, it's all yours.

**Lynn:** Thank you, everyone. BioWorld does a lot of analysis related to the business development transactions that evolve the whole drug development market, but it's important to remind everyone that it's all related to the most innovative therapeutics in development. It's about improving the human condition, helping to cure diseases, improving quality of life, and extending our healthy lifespans. All of that requires financial backing and impacts the rise and fall of amazing scientific advances.

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