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**Voice-Over:** The *BioWorld Insider Podcast*.

**Lynn Yoffee:** This is the *BioWorld Insider Podcast.* I'm Lynn Yoffee, BioWorld's publisher. Longtime BioWorld readers are well-familiar with the pace of daily deals and financing news. Rarely does the day pass when we're not bringing you the details of a new R&D alliance, financing, a company jumping into the public markets, or being acquired. With deals, it's $50 million here for a target discovery collaboration, a couple of $100 million there for a co-development pack.

These stories are the heartbeat of relationships between industry giants and their more innovative, always less well-funded peers, but what's the top-line read for deal-making these days? With nearly a thousand biopharma deals completed through early August amid a volatile economic climate, there's a lot to talk about. What about M&As turning out to be perhaps less vibrant than some had predicted? How are IPOs looking?

In the wake of huge amounts of government-funded, grant-making, and nonprofit deals that carried the sector through the initial years of the pandemic, we'll look at the cooldown. To cover it all, my co-host Michael Fitzhugh and I are joined by BioWorld senior analyst Karen Carey, whose data-driven research delivers a detailed picture of the ups and downs. Hi, Michael, and welcome back to the podcast, Karen.

**Karen Carey:** Good to be back.

**Michael Fitzhugh:** Thanks, Lynn. Yes, definitely. Welcome back, Karen. We're so glad to have you here. I've read a lot of your stories about financing and deal-making activity over the years. It seems like there's been a lot of deal-making activity this year. Where did a deal stand so far this year in comparison to other years?

**Karen:** Yes, Michael, it's really been a very busy year for sure, but the number of deals is actually down from the last two years. Through early August, we counted a total of 955 completed deals. When I'm talking about deals, I mean licensings, joint ventures, and collaborations. We are not including M&As. Those deals are below what they were last year and below 2020 by about 22%.

Now, on the other hand, deal values have gone up. They've gone up by 7% over 2021 and by 2% over 2020. Not huge amounts, but they are up. If you look at 2019 before the pandemic began, deal values are actually up by 23%. This is all looking at the same time period of January through early August. Now, in 2022, the 955 completed deals have a combined value of $114.5 billion. Now, that's quite a lot by historical standards.

**Michael:** When you look at the landscape of deals in the last year, what are some of the recent deals that stand out to you?

**Karen:** Yes, sure. One of the largest deals this year announced in August, it is worth $6.2 billion between Poseida Therapeutics and Roche to develop allogeneic CAR T-cell therapies for haematologic malignancies. In fact, immunotherapies, they continue to be a major driver of deals. It's not only CAR T-cell, but RNA technologies as well. Skyhawk Therapeutics, for instance, signed a $2.05 billion partnership in July with Sanofi for RNA modulators using the SkySTAR platform for cancer.

Pfizer and Beam Therapeutics, they signed a $1.35 billion deal in January using RNA technology. Acadia and Stoke, they have one that's just under $1 billion. A few weeks ago, there was also Orna Therapeutics signing a $3.65 billion deal with Merck for a circular RNA protein expression technology. As for CAR T, Bristol Myers Squibb has signed on with Immatics and Century Biotherapeutics. Those are $4 billion and $3 billion deals.

What is interesting about Bristol Myers Squibb as well as Sanofi is those two companies are involved in 8 of the top 12 deals so far in 2022. Sanofi has the number two and three deals with IGM Biosciences and Exscientia for about $6.2 billion and $5.3 billion respectively. BMS has numbers four and five with a $5 billion Evotec deal and a $4.3 billion Immatics deal. Now, the Poseida-Roche one I mentioned earlier, that is number one. It's slightly more than the Sanofi-IGM deal. Most of these top deals are targeting cancer, but some are also focused on immunology and infectious disease.

**Michael:** The pace just seems to be picking up. These billion-dollar deals were really a rarity a while back. Now, they're not. I don't know. Maybe too far to say that they're plentiful, but there's a lot more of them. What's driving that?

**Karen:** Yes, Michael. Years ago, we never saw these, but the industry was younger and the technology newer. Now, we're on the brink of really making huge differences in the lives of patients. Huge in terms of curative differences. We know the immunotherapies don't work for everyone, so there's some research to be done there, but they work really well for others. Cell and gene therapies can truly transform the outlook for patients with rare diseases or those with no other options. The deals are getting bigger because the payoffs are bigger, not just for patients, but for the companies that are developing these transformative technologies.

**Michael:** I just want to interrupt you for a second because that payoff element obviously is very much in the headlines recently with, I think, a therapy that we're going to talk about next. It's really transformed the conversation around what therapies can bring to the table, how they're paid for. That conversation has been in the headlines, especially around bluebird bio. Tell us about that.

**Karen:** Right, exactly. Bluebird bio, they just got approval for Zynteglo on August 17 for treating transfusion-dependent beta-thalassemia. Now, the wholesale acquisition cost is $2.8 million. That's astronomical and, quite possibly, the most expensive drug to date, but you have to put it in perspective. It's a one-time IV infusion and it could save lifetime medical costs of $6.4 million.

Now, that's according to the company, but the company has also said it would reimburse payers 80% of the cost if the therapy doesn't keep a patient transfusion-independent for two years. The payoff of these therapies is huge, but they have to work too. When we're talking about the billion-dollar deals, where exactly are we right now? Through August 24, I counted a total of 46 deals worth $1 billion or more with a combined value of $86.8 billion.

Now, that's about 68% of the total deal value this year. If you compare to all recent years, it is somewhat in line with what we saw in the last two years, but it's tracking ahead of all previous years. If you go back each year, there are fewer deals and they are worth less each year. In the full year of 2016, for example, there were only 20 deals worth $1 billion or more with a total value of $39.3 billion. That is less than half of what we're seeing in the first eight months of this year.

**Michael:** Wow, so let's talk about the broader picture against the backdrop of this big dollar-deal activity. You recently reported that deal values were down by 67%. What's happening with M&As? Why are there so few combinations out there? We expected there were going to be a lot.

**Karen:** Yes, well, I think what's happening is companies are trying to hold onto their value. They are opting for licensings and collaborations over M&As. A lot of companies, they're well-financed also. We just came off two of the top financing years in the history of biopharma. Companies do not necessarily need to exit yet through a sale. They may be waiting for more mature technologies when they can command a higher price tag. As of the first week in August, we had a total of 56 M&As valued at $25.7 billion.

The numbers in 2021 were 95 M&As worth $78.5 billion. That's during the same time frame. Not only has the value fallen by 67%, but the volume is down by 41%. Even if we go back to 2020 and the pre-pandemic years of 2019 and 2018, we are still way down. This isn't because of the pandemic. That's not to say that there haven't been some big M&As this year. Pfizer's March buyout of Arena Pharmaceuticals for over $6 billion is the biggest this year. Pfizer also has a pending deal to acquire Biohaven for $11.6 billion.

A lot of this M&A activity is coming from Pfizer's $37 billion in proceeds for its COVID-19 vaccine, Comirnaty, in the last two years. They made a lot of money off that vaccine. Another big M&A. Bristol Myers bought Turning Point for $4.1 billion. That one just closed, August 17th. There are still some big ones being announced. Novo Nordisk just yesterday said it would buy Forma Therapeutics for about $1.1 billion.

Now, I'm calling $1 billion a big M&A, but when you look at some others through the past years, it's actually not that big. I have heard it said that most of the biggest companies that can command the highest prices have already been purchased. Once you take Celgene, Alexion, Immunomedics, and Allergan out of the mix, these were M&As between $21 billion and $74 billion. Once you take them out of the mix, there are only so many others that can drive up the value of M&As significantly for a given year.

**Michael:** It is a real testament to the amount of work that goes into building the value of these companies, the amount of research, and the transformative work of actually taking the research into commercial application. It's one of my favourite parts of our job is seeing that transformation all along the way in the trials. Obviously, there's a fair bit of attrition along the way, but it's just remarkable. Let's start at the financial markets. We've certainly seen sharp declines this year in stocks and less money being raised as well. How is that affecting the industry overall?

**Karen:** What we are seeing, I think seems to be a correction of the intense enthusiasm, the zeal for biopharma during 2020 and 2021 when nobody knew what was going on with COVID. Biopharma seemed to be the world's best bet. What we had was a lot of generalist investors putting their money into biopharma stocks that were becoming considerably overvalued. There was a time during the pandemic when the broader markets were way down and biopharma was way up.

Now, they are showing the same path, which seems to be a much healthier state. Although many stocks are still down this year, I noticed they have begun to rise over the summer. If it keeps going in that direction, maybe they will rise above the end of last year. We'll have to wait and see on that. As for financings, again, with the enthusiasm of the last two years, it's not really a fair measure.

Yes, financings are down. Specifically, IPOs and follow-ons. As a whole, they are not down that much in comparison with pre-pandemic years. As of last week, the industry has raised $37.8 billion. That's slightly more than the $36.9 billion raised in the same period for 2019, yet both 2020 and 2021 had raised more than double, upwards of $84 billion by this point. We're just returning to the pre-pandemic days.

What we do see, however, is a shifting of financings in which a larger proportion is being raised through venture capital rounds. The $14.9 billion raised so far this year through VC is above both 2019 and 2020, although it is still slightly behind last year. Also, IPOs and follow-ons, they have raised the least when comparing it with each of the three prior years. This year, it is at about $12.4 billion.

**Michael:** Let's talk a little more specifically about IPOs. You recently reported that IPOs are significantly down, but that the 2022 crop of stocks are doing well. The companies that went public in 2020 and 2021, not so much. What's going on with that?

**Karen:** Yes, so we just did an analysis of IPOs conducted on US exchanges this year. That showed that the stocks have risen by an average of 7%. Now, this involves just 12 IPOs because we didn't include those involving American depository shares or units or those done on foreign stock exchanges. This was only US and there are only 12 this year. That is all. Looking at 2021, there were 90 of these IPOs completed.

**Michael:** Wow.

**Karen:** Yes, so that's quite a difference. That's for the full year of 2021, 90 of the IPOs completed. As of the August 15th closing price, the August 15th of this year, those IPOs are down 42%. If you go back to the IPO crop of 2020, there were 74 done. Looking at that August 15th closing price, they are down by 34.6% on average. Now, a few things may have been going on to explain this.

For one, investors were extremely receptive of biopharma opportunities at the onset of the pandemic and throughout 2021 as cases and deaths kept rising, mutations created the need for new research. Companies may have commanded prices higher than what they could have achieved in a typical environment, but there was a lot of uncertainty. The broader markets were suffering. There was a new US president in 2021.

There was Delta, there was Omicron, there was waning immunity, and a lot of questions of how will this affect these companies and their stock prices if there are lockdowns again. Then on top of the pandemic, we have the economy and gas and food prices. We have the war in Ukraine as well as efforts to control drug prices and a World Trade Organization intellectual property waiver.

For all of the stocks that debuted this year, investors already knew these things. For the IPO stocks of 2020 and 2021, things were not quite so clear. Many of the investors were generalist investors who maybe did not have the strongest pulse on the biopharma industry. For companies, that is a disadvantage of coming out too strong. There's only one place to go and that's down.

The other thing I would say about this is some of these companies with struggling stock prices, they now have enough money to carry them through the next two years, hopefully to the next inflection point. There is an argument that companies should raise money when they can, when it's readily available, whether they think they need it or not because you never know what could be around the corner. You got to get the money when you can.

**Michael:** Wow, that's a really substantial list of factors and complex too. It's interesting, I think, that another factor may have been that there were so many companies that went public with just preclinical programs. Do you think that that might have been an omen as well?

**Karen:** Absolutely. Some of the technology is very early and so it's not surprising that the stock prices wouldn't be going high. Those companies probably saw an opportunity and they grabbed it. Yes, there's definitely a lot more preclinical companies that are going to the public markets.

**Michael:** In addition to financings and deals between biopharma companies, the BioWorld team tracks biopharma company deals with nonprofit and government entities and grants as well. Have we noticed any new trends with those this year?

**Karen:** I don't know that it's so much this year, but the big trend we began to see was back in 2020. Governments, primarily the US government, began to throw huge sums of money toward biopharma companies for the development and supply of COVID therapeutics and vaccines. For the second week of August this year, BioWorld tracked 439 bio nonprofit deals worth $6.6 billion.

A lot of that is going toward COVID efforts, including $3.3 billion in June for BioNTech and Pfizer and $1.74 billion in July for Moderna for the supply of their Omicron-specific vaccines. Now, these are the BA.4, BA.5 boosters that were just authorised. There is also another $1 billion going to Eli Lilly and Company for bebtelovimab. With grants, there have been 200 worth $954 million this year.

More than half of the funds, about 54%, are coming from US government sources. The largest grant this year is an NIH grant for PostEra to use artificial intelligence to develop small molecular antiviral therapeutics. Now, we recognise that different countries may have different requirements for the disclosure of grants and deals, but this is what we have found based on our coverage of what is disclosed.

When we compare 2022 to last year, both grants and bio nonprofit deals combined are down by more than a quarter. The value of the grants and deals are down by 22.8%. Now, that is as a whole. When you look at just deals and grants focused on COVID, there's a 61% decrease in volume and an 18% decrease in value. There's still a lot of attention on COVID, but it is lessening. I think we can probably take that as a sign that the world is getting back on track.

**Michael:** Lynn, as BioWorld's publisher, you really have a bird's eye view on these trends, both from the biopharma and the med tech side. Do you have any questions about how things have been unfolding?

**Lynn:** I do, Michael. Karen, I'll ask you to kind of take a step back yourself. This is a lot of data. For our listeners out there, you can find all the data and Karen's astute analysis on the website in our daily news feed. Karen, tell us, with all of this money, the billions of dollars flowing into the biopharma sector. As an insider, we would say it's healthy. The sector is healthy and it's rocking and rolling, but are patients benefitting? How is this affecting humanity? Are there better drugs? You mentioned earlier that there are more curative drugs out there. What's your overall sense about how humanity is benefitting from the billions of dollars that are flowing into this research and development?

**Karen:** I do think that sometimes you have to take a lot of small steps to get to a position in which you are really benefitting patients. I remember years ago being at a conference and some scientists put up on the screen, a stage IV lung cancer patient that was treated with immunotherapies. I went up to speak to the scientists afterwards and I'm like, "Well, after the therapy, how much did it decrease the size of that tumour?" He told me it was completely gone.

He had stage IV lung cancer and the tumour was completely gone at the end. Yes, there's billions of dollars going into the industry, but I do think this is very transformative. I do think that the mRNA technologies and what they've done for COVID, that can be used toward cancer, which is what it was initially being developed for. I do think we're going to see some dramatic changes in the industry going forward. We're going to understand why all this money is swirling around biopharma.

**Lynn:** Okay, but right now, FDA approvals are down by a third and we're not seeing as many new molecular entities being approved. When do you see this turnaround happening that you just mentioned? People always want to-- that kind of look into your crystal ball and where is this investment taking us? Are we talking 10 years from now or 5 or 2?

**Karen:** Yes, that is so difficult to really say when it could happen, but I am constantly surprised at what we're able to do now compared to what we could do 10 years ago. FDA approvals are down. We did notice that. They're down 30% in comparison with last year. NME approvals have been cut in half, but we also noticed that the filings were down too. It seems like there's fewer drugs that are on our PDUFA list, our drugs-on-deck list if you will. There's only 84 on there right now. Whereas last year, we had about 119 on that list.

The clinical data is down. We have noticed some of these things. All I can say is it starts with an idea. They move the idea into preclinical testing, then it gets funded, goes into clinical testing. You have to go through the steps to get these therapies approved. We still see that 90% fail, but 20, 30 years ago, we didn't have a cure for a stage IV lung cancer patient. Like I said earlier, the immunotherapies don't work for everyone, but that's a pretty big deal for the people who they do work for.

**Lynn:** That is a good example and fair enough. I really appreciate your assessment there. I know it's hard to look into a crystal ball, but you've got that broad picture with all of the data that you pulled together and digest on a regular basis for the team and for our readers.

**Karen:** Thanks. Thanks, Lynn.

**Michael:** Thanks, Lynn, and thank you, Karen, for joining us. It's been really fantastic to get this overview of the industry and where we're at. I'm going to pass things back to Lynn to wrap us up.

**Lynn:** Thanks, Michael. Thanks, Karen. As always, you can come to bioworld.com to find all of this data and analysis. We'll continue to keep you informed of all the most important scientific, clinical, and business updates. That's our show for today. If you need to track the development of drugs, turn to bioworld.com. Follow us on Twitter or email us at newsdesk@bioworld.com. Also, if you're enjoying the podcast, don't forget to subscribe. Thanks for joining us.

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**Voice-Over:** BioWorld, published by Clarivate, is a subscription-based news service, but all of our COVID-19 content, more than 7,000 articles and data entries since the start of the pandemic, are freely accessible.

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