Sarah Emond
It can't be that we continue to just be price takers from the ecosystem without any conversation about whether or not the price is fair or we won't have money to pay for these innovations in the future.

Ellen Kelsay
That's Sarah Emond, President and CEO of ICER, the Institute for Clinical and Economic Review, joining us to provide an update on the market for cell and gene therapies, some of healthcare's most innovative and costly treatments.

I'm Ellen Kelsey, and this is the Business Group on Health podcast, conversations with experts on the most relevant health and well-being issues facing employers.

We spoke with Sarah about the cell and gene therapy landscape back in 2023. Today, the market is entering a new phase, shaped by challenging evidence and evolving questions about sustainability as treatment indications expand.

Sarah, welcome back to the podcast.

Sarah Emond
It's such a pleasure to be back, Ellen. Thank you.

Ellen Kelsay
Yes, well, to our listeners who are familiar with you, they probably remember a couple years ago you joined us, and the more things change, the more they stay the same. So here we are again, talking about cell and gene therapies. As you know, we just released our annual Employer Healthcare Strategy Survey last week, and many of the findings in that are probably going to be laced throughout our conversation today about healthcare trend, affordability, drivers of that, and in particular, what's going on in the pharmaceutical space, and even a further drill down relative to cell and gene therapies. We'd love maybe just to get your thoughts as we open up the conversation today, kind of your reflections on the macro level, and what do you see going on, and any insights or nuggets from our survey that caught your attention.

Sarah Emond
Well, your survey was fantastic, even if it was slightly depressing, which I think is probably a common reaction. As I was thinking about the survey results and talking about cell and gene therapy, our topic today, it was three years ago that we were talking about these issues of how we have an affordability crisis. We need to act urgently to address it. There needs to be action on all sides, from the purchasers, to the payers, to the manufacturers, to figure this out and service to more affordable access for patients. I can't help but be pretty bummed out by the results of your survey because we're going in the wrong direction. As we talk today about where we are with cell and gene therapy, I still have this same feeling from a few years ago of tremendous science, science fiction level ability to change genetic challenges in human beings, and yet a system that is still struggling to figure out how to afford these innovations. So we will need to continue to highlight this issue to make sure that people are thinking about how to act urgently to ensure access because I don't think there's enough of an appreciation right now for how delicate this balance is.

Ellen Kelsay
All right. Well, let's get into it because we've got a lot to talk about. Okay, so let's rewind the tape. Three years ago when we last spoke, as you said, there was all of this momentum, a lot of enthusiasm and optimism about what could be accomplished in cell and gene therapy, a lot of activity in the pipeline, and we thought we'd be at a different place. That didn't really necessarily

pan out the way that we thought. What happened? When you look back over the past few years, where did things go sideways?

Sarah Emond
I see it in a couple of different areas. One is just in the ability of the status quo to just continue. And so now I am speaking directly to purchasers, people charged with providing health insurance to large numbers of people, whether they be large employers, small employers, medium-sized employers, governments, etc. What I noticed three years ago still continues. There's a lot of, oh, I don't have to worry about gene therapy yet. It's not hitting me. If I'm a medium or a small size, there's still not that many of them and so I'm just going to roll the dice. Or maybe they've got some reinsurance or some stop loss and so things are okay right now. Or I'm a big employer. I can kind of absorb these costs. I'm not going to worry about it too much. So one bucket for me is some things that changed, but not a ton of innovation and evolution about how to pay for these therapies. The second thing that's happened is I don't think anyone predicted the regulatory uncertainty that was going to come, especially around cell and gene therapy. Things like the commissioner's priority review voucher, which were introducing new pathways for approval that were introducing their own regulatory uncertainty on top of decreased NIH funding. All of that together has meant that we are not where we expected to be when we were talking three years ago. The number of approvals is pretty steady. We expected it to go up. The access issues continue for certain patients. Pricing decisions made by these manufacturers that are not in line with value, which is putting stress on the entire ecosystem to ensure access. There's been this intersection of several different forces that have created the scenario we're in, which is we're not really where we had hoped to be three years ago.

Ellen Kelsay
Well, you've got a crystal ball. I'm giving it to you right now. When you look the next 3 years ahead or even the next 5 years ahead, what do you see in that crystal ball and what should employers expect? What might change of that confluence of forces you just mentioned? How might they evolve?

Sarah Emond
I still remain optimistic that we will figure this out. We will have payment mechanisms that support an innovation ecosystem and getting patients access in a way that is affordable. I am encouraged by some of the calming over at the FDA of late. It looks like there is at least more predictability than there has been in the last 18 months. That's a positive for me. We have seen some gene therapies get approved. We've seen some gene therapies get favorable treatment from advisory committees and so that's a step in the right direction. But as I look at the pipeline, the good news there is it's still pretty robust. While we haven't seen the big increase in number of approvals that had expected, we do still see a robust pipeline. Now, predicting when drugs will be approved is impossible, it turns out. But if I'm looking at some of the data that we have, I think you can expect to see some follow-on therapies in areas we've already seen gene therapies, things like sickle cell disease, hemophilia, a form of blindness called retinitis pigmentosa. You can continue to expect some gene therapies in rare disease. We've seen things for Febreze disease, Huntington's, Duchenne muscular dystrophy, ALS in the pipeline. What's really interesting, especially for this audience, is to keep an eye on gene therapies for more common conditions, high cholesterol, wet age-related macular degeneration. That's going to be another test for our system in terms of how we pay for potentially curative therapies for large populations. Those are some of the things that are on my radar.

Ellen Kelsay
All right, because I wanted to ask you, you mentioned at the outset that some employers just, you know, it was more theoretical. They didn't think that they would really have high odds of somebody on their plan needing one of these. Or if they were the very largest, it would be one or

two people and financially their plan could absorb that. Now you're talking about, the point you just made, many more people within the population who potentially could be eligible, high cholesterol was an example you gave. There are a lot of people walking around who have high cholesterol. How is an employer to think about that from a coverage perspective when they have perhaps much wider swaths of their population who potentially could benefit from these therapies?

Sarah Emond
I think it's going to be important for purchasers to have very good partnership with their payers and their PBMs on this because clinical eligibility is going to be a really important part of managing access to gene therapies for more common conditions. Because guess what? Yes, a lot of people have high cholesterol, but statins are terribly effective at treating high cholesterol. It's not going to be that everyone with high cholesterol should get a gene therapy. I think there's going to be an important recognition of knowing exactly for which patient populations, even if they are for a larger patient population. It's also going to demand a conversation about price, not just price for the gene therapy, but for the totality of healthcare spending. We could just take the drug spend portion, the 20-25% that's going to drug spend. One of the reasons we all are feeling tension in the system, and I use the word all here because ICER is a small business effectively, and I have had health insurance premiums also go up, and so we experience it. But one of the things that we're experiencing is that generally we're overpaying for value when it comes to our prescription drug spend and so we feel like we don't have anything left to spend. So when a new therapy comes on the market that might be priced appropriately in the millions of dollars because it's a tremendous therapy, we feel tension and we feel an affordability crunch. I think that as some of these gene therapies come to market for larger populations, we are really going to need to be faced with, okay, well, why am I paying $480,000 for a new pancreatic cancer drug? Is that the right price? If that was priced to value, would I have more money in my drug spend to help patients with high cholesterol who aren't controlled on statins or PCSK9 inhibitors? These are uncomfortable questions, but this is what's coming and it can't be that we continue to just be price takers from the ecosystem without any conversation about whether or not the price is fair, or we won't have money to pay for these innovations in the future.

Ellen Kelsay
I want to come back to the pricing part of this equation in just a few minutes, but you mentioned about clinical eligibility and having rigorous standards and clear standards around for whom these therapies would be appropriate. Leads me to my next question. Are the current care delivery models prepared for this? Do care teams understand what rigor needs to be in place? How do you see the entire ecosystem responding, either effectively or not, to the broader population interest in some of these therapies?

Sarah Emond
I think it's evolving. I think you see pockets of centers of excellence that are doing a fantastic job standing up entire divisions to deliver gene therapies and cell therapies, and they're able to handle everything from the prior authorization to the payment to travel support for the patients, and there's pockets of that coming up. But that is working right now, given that we only have 40 gene and cell therapies, and so that's a manageable number for the ecosystem that exists. So provider capacity is really important here. It may be true that it has been a rate-limiting step for the uptake of some of these medicines, that you have to travel to one of these centers of excellence. Not every patient wants to do that. Not every patient has the ability to take time off in order to access a therapy, you know, 100, 400, 600 miles away. I think that there does need to be recognition of the provider capacity needs to improve. I'm optimistic here because there are people who are working on this, and there's different organizations, some organized as for-profit businesses trying to help purchasers navigate this ecosystem, but also researchers and academics

who are expert in the delivery of gene therapies who are trying to figure out the ways that new technologies like telehealth and AI can help expand access so that it's not just at these centers of excellence. But you're absolutely right to bring this up. Provider capacity is a huge component of this.

Ellen Kelsay
You talked a little bit about ICER earlier, and one of your core functions is evaluating evidence. So question is, are there therapies where the evidence may have changed over the years? Curious as you all take a look at this, how frequently do you look at the evidence and as you're monitoring, you know, more time in market, more evidence, which therapy classes now have the strongest evidence and maybe where are we not seeing the evidence prove itself out?

Sarah Emond
I would say this is an area where we're still waiting for more data, generally. There are some specific examples of where we've seen some great information. This also goes back, if you don't mind, a quick tangent into the different ways that things come to market through the FDA. A lot of gene therapies have been approved through what we'll just call traditional approval. They've conducted clinical trials showing an impact on an important clinical endpoint, and then they get the approval. We also have some gene therapies that have been approved through accelerated approval and this is the idea that they're approved on a surrogate marker, something that might predict clinical benefit, but we're not sure and so we need to keep studying it. I think that's where there has been some open questions. So Elevidys comes to mind for Duchenne muscular dystrophy. Needed to conduct an additional trial in order to see if the drug was doing what it intended, helping patients with Duchenne. The results were mixed at best. I think that in some ways, the phase three trial did not meet its primary endpoint, and it left a lot of people questioning. There was some additional data that came out. But that's an example of where it's really hard as a purchaser to try to navigate that, because how to understand a surrogate endpoint and its impact for patients and then confirmatory trials as it comes later can be really difficult and we are happy to play a role in that ecosystem as experts in evidence adjudication. I will say that in other areas, the big question about gene therapies is how long do they last? There is a biological plausibility that you only need to get the gene therapy once. If it's replacing a gene that isn't functioning and then it's producing the protein correctly, could that work forever? We don't know. We are just about to get, for some of these gene therapies, our data on durability of effect and that's a really important part of navigating this ecosystem. It's one of the reasons I really like outcomes-based contracts in gene therapies, when I don't always love them in every other circumstance. Because if the gene therapy stops working for the patient after a period of time, having an agreement that some sort of refund goes back to the purchaser just makes a lot of sense, and I think can ease access to some of these therapies. So durability of effect is another area we are watching closely. We'd like to know if these gene therapies work for 5 years, 10 years, 20 years and given that some of them have been on the market now for about 5 years, we are starting to get some of those data.

Ellen Kelsay
This is really all getting to the question of value, which is another one of your core functions at ICER. Clearly, as you've just articulated, evolving evidence should impact how plans think about payment for these therapies or even some of the contractual and alternative payment models they might want to consider. You mentioned outcomes-based contracts. Anything you would offer in this kind of discussion related to value, payment, alternative contractual and payment methodologies?

Sarah Emond
Yeah, I think that the 101 here is that the price should be aligned with an independent assessment of value. That means a price that's linked to how well we know the drug works at that moment.

That can reflect any uncertainty we have in the data set, uncertainty about durability of effect, uncertainty about an adverse event, and uncertainty about effectiveness. That can all get wrapped up into an analysis, and that's what ICER does. So if you start with what ICER says the fair price is, and then add on an outcomes-based contract, I do think that's a really good starting point for trying to ensure affordability and fairness from the price and access perspective, where there is still some debate or some of these other alternative payment models that have been discussed. I'm really interested in watching some of the companies that are trying to do this. Everything from risk pooling, like instead of a purchaser actually having policies for each gene therapy, the purchaser just pays a per member per month to be part of basically a health plan that just does gene and cell therapies and then you don't have to worry about anything. You pay your PMPM, anyone in your employee base who needs access gets access, right? So that's more of a risk pooling approach. There's also an approach of trying to manage the journey of the patient. So someone like an emerging therapy solutions, ETS, they're actually saying, well, hey, if I'm going to identify the patients who might be eligible, we're going to talk to them about whether or not they want a gene therapy, and then we're going to help them through their whole journey and that might mean going to a centers of excellence, etc., and then there's a way that you're ensuring the right patient is getting access to the right therapy at the right time. There are these really interesting models developing. I don't know that we have a lot of data about which of them are working great. We do have a white paper about this from a couple of years ago where we talk about all the pros and cons of some of these options. I know it might feel a little like throwing spaghetti at the wall, but these are still very new therapies in terms of asking society to pay sort of an upfront cost for something that's potentially curative, or at least has a long runway of effectiveness. I think it's okay to be experimenting still a little bit.

Ellen Kelsay
There's a lot that I just wrote down that I want to double click on. I might not get to it all, but maybe first is a very basic question. You said purchasers should start with ICER's assessment of the fair price. Do you all do that for every single cell in gene therapy, and if so, how quickly are you able to put that information out so that purchasers could make informed decisions?

Sarah Emond
We're approaching a 50% rate of looking at gene therapies. I had my team pull it up between cell and gene therapies. We have not been able to look at every single one just because of capacity given our size. We do take some of our team like to call it the Cadillac approach. It does take about eight months to do a review and that's because stakeholder engagement and public engagement and public comment is so important to us and so important to the process. So what we do try to do is pick a topic before it's FDA approved with hopes that our work comes out right around when we expect FDA approval. That's what we've been able to do with the 13 cell and gene therapies that we've looked at so far. We also have to make choices. Sometimes we're looking at what we think are going to be the therapies that are going to get the most attention, maybe have a bigger patient population or a real paradigm shift. Some of the therapies that have come have been for very small populations, and so that might not be as important as some of the others. But I think generally you get a sense by being able to look at the ICER reviews, it's about 70% of the time we see the price is actually fair for these therapies. That's the exact opposite percentage of the entire suite of drugs that we look at. It's about 70% of the time that the price isn't aligned with value. So it's funny to me that a lot of times these prices are actually reflective of the value, and then we're really talking about a payment problem and how do we pay for all of that value up front given our system's not used to that. But we do prioritize looking at cell and gene therapies, and we'll continue to do so because we do think a lot of purchasers and other decision makers find it helpful.

Ellen Kelsay
That's great and that's an important distinction. I'm glad you clarified that. My other follow-up question had to do with the durability of effect, and I think that's an incredibly valid point, certainly as an employer who's considering an outcomes-based contract. But you also mentioned it could be 5 years, it could be 10 years, it could be 20 years. So as an employer is building out an outcomes-based contract, how do they know which time frame to specify to really understand durability?

Sarah Emond
Well, it's also the question of feasibility. It's not going to be feasible to have an outcomes-based contract that's probably any longer than 5 years, and that's the reality of the system as it exists right now. I think if lived in a different system, maybe we could, and we can imagine that day, maybe. But it's difficult to ask a manufacturer to go at risk for that amount of time. It's difficult for a purchaser to carry that amount of risk and uncertainty, depending on how it's structured, how that might even look on their books becomes a consideration. So I think 5 years is probably the longest you might see an outcomes-based contract. That might be tricky because the durability might only last six, and that might feel really unsatisfying that you had a 5-year contract and it was working. But that's also something you can do in the modeling about what the price should be. A price can also reflect when you think the drug will stop working for that patient. So that's why I think it's important not to just talk about outcomes-based contracts, but to talk about that independent assessment of value and that fair price, because then you can have a price that's reflective of that uncertainty. If you don't think there's any reason to believe it's going to work longer than 5, 7, 8 years, you can put that into the price calculation and then have extra protection with the outcomes-based contract. But everything I've been hearing from purchasers is this is the hard part and negotiating these contracts, depending on the manufacturer, it can go well or not so well. There's differences in how manufacturers are approaching this. I've heard about challenges keeping track of patients because your employee might leave and go to a different employer and a different health plan administrator. So then you're having challenges about whether or not the patient is still responding to the therapy. I think there's some opportunities to handle this and I know some purchasers are doing that, and again, with the smaller populations that are eligible for a lot of these therapies right now, that's a little bit easier. I acknowledge that gets harder when you have more gene therapies approved and lots of different outcomes-based contracts that you're trying to adjudicate and then more patients that are moving between your company and a different one. So there's some challenges about the outcomes-based contract approach as we get more gene therapies approved, that's for sure.

Ellen Kelsay
Well, you also mentioned fair price and that most of your studies do show these are priced fairly, but it's more so a payment challenge. There's also, you know, to be fair to the manufacturers, they're funding the research, they're having to go to market, they've got a lot of other complexities they're contending with. What are some of the other challenges that are facing manufacturers?

Sarah Emond
Between the regulatory uncertainty and just how expensive it is to develop a new medicine, their plate is full of challenges. I recognize that and understand that. I spent a decade in industry and I know how hard this is. I do think there's an opportunity to recognize that as part of a balanced innovation ecosystem. We have to acknowledge this isn't easy. If it was easy, we would have figured all of this out a long time ago. But we demand a lot from the manufacturers in terms of proving safety and efficacy. It is not cheap and then we do want there to be enough of a financial reward at the end that we have an innovation signal that says, let's develop more of these potentially curative therapies. So we need to balance that. What's been challenging is when you

have outliers to what is generally a well-meaning ecosystem of manufacturers trying to do right by developing good therapies. When you have therapies that come to market with big price tags that don't have any evidence of effectiveness, that can really sour the entire ecosystem. One thing I've been calling on manufacturers to do is to really be leading with their own voice about what they want out of the ecosystem. They want a rigorous FDA, most of them. They want to be able to stand behind the safety and efficacy of their products. And more leadership from manufacturers on, hey, yeah, we did the right thing. We ran a great trial and here's the evidence that shows that this is transformative for patients can be met by a payment ecosystem that says, great, and we're going to reward you for that. Where we fall down is when a manufacturer might bring something to market with scant evidence of effectiveness and maybe even evidence of harm and then they're still asking the ecosystem to pay a lot for that. That's the imbalance that I think is having a negative impact on how even some purchasers think about this entire space.

Ellen Kelsay
Well, the regulatory environment, as you started out the conversation, there's been some uncertainty in recent years. You just mentioned more rigor from the FDA. Any other developments, either good or bad from the regulatory perspective, that would be ones to keep an eye on in the coming years?

Sarah Emond
Well, sort of adjacent to regulatory is just the government approach to this issue that we've been talking about, how to manage pricing, access and affordability. I was excited to learn that the CMMI models, so that's the Center for Medicaid and Medicare Innovation at CMS, continued in this administration. So these models were designed to help deliver access to the sickle cell gene therapies to Medicaid departments. A majority of Medicaid departments signed up and there is now a team at CMMI that has negotiated outcomes-based contracts with the two manufacturers for the sickle cell therapies and they are adjudicating those contracts. They're tracking the patients. They're making sure that there's refunds if necessary, if the gene therapy stops working for the patients. This model is worth watching. This idea that a federal agency can take on some of the administrative burden of these therapies is not only attractive to Medicaid programs, I think it might be attractive to some purchasers too. So I think that's definitely one to watch. I'm interested to see the outcomes, how patients are doing through the program, how many patients have gotten access, has it been cost-effective, how have they sort of managed the price and the outcomes-based contracts. So that's one to watch. I think the other thing that I would watch is just over the next 6 months or so, probably 6 to 12, there are some gene therapies and cell therapies in the pipeline that we would expect to hear from the FDA and I think that it's worth watching to see what kind of approvals or rejections we get. Given the uncertainty of the last 18 months, but the hopefulness that we have in this moment that things are a little more calm, it will be helpful to know how this version of the FDA is seeing the gene therapy landscape, because that's going to have impact on the purchasers, of course, and thinking about what therapies are in front of them that they may need to pay for, but then also back to that innovation signal. Are we sending a healthy innovation signal back to the manufacturers so that the next wave of gene therapies gets developed?

Ellen Kelsay
Great. Okay and you said that's the next kind of 6 to 12 months.

Sarah Emond
Six to 12 months, I would say.

Ellen Kelsay
Well, let's talk about when you think about the future, what gives you the most excitement, sense of optimism? Where do you think the most promise holds in this field over the next maybe 6 to 12 months?

Sarah Emond
The science is really tremendous. I'm a biologist by training. I worked at a genomics-based drug discovery company that was sequencing the human genome in the early 2000s. I am thrilled that that scientific discovery is leading to therapeutics that are addressing the underlying genetic cause of so many diseases. I think we're figuring this out. The number of purchasers who have this on their radar has increased and that's a good first step to try to figure out solutions. The pipeline is robust. Manufacturers want to do right by the science and by patients, and they are, in this space I can say, I think, a lot more interested in conversations with government, with purchasers. The fact that both of the manufacturers of the sickle cell products said they would participate in the CMMI model, I think, tells us something about the willingness of the industry to try to figure this out. I do have optimism that at the end of the day, we all want the patients with a particular condition that might be treated by one of these therapies to get access. We all have a common starting point. We are seeing what happens when there's real conversation about how to bridge the affordability gap, the uncertainty around the evidence, maybe through some pricing and some outcomes-based contracts, but just also in a willingness to try new things instead of just saying, okay, we're not going to cover cell and gene therapies, which I heard that more a couple of years ago than I hear that now, and so that gives me some optimism.

Ellen Kelsay
I agree so much with you. I think a lot has changed for the better. We do have a greater awareness. We do have different models. You mentioned CMMI. You mentioned risk pooling. People are accepting outcomes-based contracts more than they probably would have even considered a few years ago, so we are certainly moving in the right direction, and as you said, these are unbelievable therapies that for many are curative or life-altering, so we all want to support that and need to continue to strive to find ways to pay for them. Sarah, it is always a pleasure to have you on. Just so greatly appreciate your knowledge, your insight, and the great work that you and your team are doing at ICER. Thanks so much.

Sarah Emond
It's been an absolute pleasure, Ellen. Thank you for having me back.

Ellen Kelsay
I've been speaking with Sarah Emond about the evolving challenges and developments and what employers should be watching as the next generation of cell and gene therapies comes to market.

I'm Ellen Kelsay, and this podcast is produced by Business Group on Health, with Connected Social Media. If you liked the episode, please rate us and leave a review.