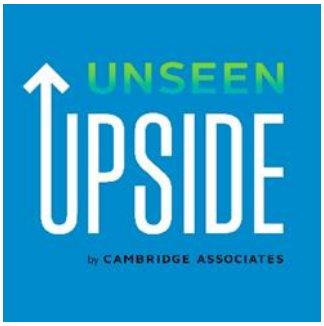

Season Five: Episode Two
Drug Affordability: The High Cost of Healing
Launch Date: October 22, 2024

[MUSIC]

Hillary Ribaudo: Recently, my husband and I found out that our two-year-old son has asthma—it's a condition affecting over 27 million people in the U.S. Given how common it is, I was shocked when the two medications he was prescribed cost me $350 at the pharmacy.

A 2024 study by RAND, a non-profit research organization, found that prices for brand name drugs in the U.S. in 2022 were about three times higher than in other countries.

So, how are drugs priced? And who shoulders the cost of creating them? In this episode, we'll hear from investors who navigate these complex decisions.

Peter Kolchinsky: There are certainly wealthy people that invest themselves, those are angels. But it's basically society's money. Teachers and firefighters through their pension funds are risking their capital on these kinds of projects.

[MUSIC]

Hillary: I'm Hillary Ribuado, and this is Unseen Upside by Cambridge Associates, where we explore investments beyond their returns. This season, we're diving into health equity, and today we're exploring the high cost of prescription drugs and some of the variables that just might hold the key to making drugs more affordable.

[MUSIC]

Boomer Esiason video: *…final seconds. And Esiason looking for the end zone…*

Hillary: In 1993, NFL quarterback Boomer Esiason was having a great year. He had a family with 2 kids and had just been traded to the New York Jets from the Cincinnati Bengals.

Boomer Esiason video: *Touchdown for the Jets!!*

Hillary: But that same year, his 2-year-old, Gunnar, received a terrifying diagnosis: he had cystic fibrosis.

Gunnar Esiason: Oddly enough, my dad had actually been quite involved in Cystic Fibrosis fundraising for several years at that point.

Hillary: Gunnar Esiason is 33 years old today, and he's a patient advocate living with CF. But without medication his story could have been very different.

Gunnar: When I was diagnosed, my parents were sort of put this really weird situation of having known quite intimately the prognosis for kids with CF at the time, which really frankly wasn't quite good.

Hillary: Cystic fibrosis, or CF as it’s often called, is a progressive genetic condition that makes mucus in the body really thick and sticky, instead of the usual thin and slippery that you would find in a healthy person. This buildup clogs important passageways, especially in the lungs and digestive system, and this causes serious health problems.

Gunnar: CF leads to production of mucus in the pancreas, which leads to decreased pancreatic activity. And as a result, we can't digest fats appropriately, we have to medicate it. And in my case, I actually, unfortunately, have a feeding tube.

Hillary: According to the Cystic Fibrosis Foundation, in the U.S., there are almost 40,000 people living with this disease that is caused by a faulty gene.

Gunnar: You know, as a very little kid, it didn't really occur to me that I was much different than my friends until my parents came into my bedroom at about 6 a. m. I was in first grade at the time. And they said, “Gunnar, we're going to see the doctor.” I had never gone to the doctor this early in the morning.

Hillary: It turns out Gunnar needed a special medical procedure.

Gunnar: They were about to place a pick line, which is effectively a long-term I. V. that stays in a patient from 2 to 8 weeks. We use it to administer intravenous antibiotics because part of the disease has this infectious disease component. And so, I was about to be administered IV antibiotics. But it's also around that time that I realized that my

classmates were not going through that on a Tuesday morning. They were not experiencing this scary traumatic moment inside a hospital system because they didn't have cystic fibrosis. I did.

Hillary: Gunnar spent a lot of time in and out of the healthcare system, and he often had to manage multiple prescriptions at once.

Gunnar: At the time, we couldn't treat CF very well, but we could treat the bacterial infections that I was living with. We had medications to treat the symptoms of CF with pills that I would take with meals and food. And then we also had different medications to thin the mucus that was persistent with my CF.

Hillary: But since CF is a progressive disease, as Gunnar got older, he started becoming resistant to antibiotics.

Gunnar: I basically wouldn't be able to survive without daily direct medical intervention. When I had my feeding tube placed, I was 19 or 20 years old, and it was this reality - striking moment that my life was forever going to be altered.

Hillary: By the time he graduated college, Gunnar was in a severe medical decline.

Gunnar: it was almost impossible to hold a job or have social relationships or really anything that we all take for granted.

Hillary: Then, toward the end of 2013, his doctor delivered very tough news.

Gunnar: She said to me, Gunnar, we're running out of treatment options. This is just probably how it's going to be for the next however many years. It was just living day by day. And it was a really hard place to be in.

Hillary: This day by day went on for about five years, until…

Gunnar: Back in 2018, I enrolled into a clinical trial for a medication, and when I enrolled in that trial, I was basically at the end of my road, like I had gone through treatment failure after treatment failure, years of hospitalizations and IV treatments. I basically couldn't make it from the bedroom to the bathroom to brush my teeth.

Hillary: The trial was blind, 50% placebo versus 50% active drug.

Gunnar: I'll never forget driving to the hospital that day because it dawned upon me that this would probably be my last chance, and when I got to the clinic, I dosed the drug and within 12 hours, I knew I wasn't on the placebo. The mucus in my lungs started to

change. Three days later, my cough went away. A week later, I could take the first deep breath in my life.

Hillary: The drug, now known as Trikafta in the U.S., or Kaftrio in Europe, was developed by Boston-based Vertex Pharmaceuticals. It's a triple combination therapy that actually combines 3 drugs. And it was approved by the FDA in the fall of 2019.

Gunnar's been on it since the clinical trial, and he describes it as transformational.

Gunnar: My health has been basically on a rocket ship ever since, to the point where I have a career, I have a family, I'm married, have kids.

Hillary: Trikafta is appropriate for about 90% of patients with CF.

Gunnar: It treats the underlying cause of the disease. It's a highly innovative medication and the best part about it is that it's a pill. So I take two pills in the morning and then one pill at night, and basically, the worst parts of CF have evaporated for me.

Trikafta does have a hefty price tag. It's priced at over $320,000 dollars or so at a list price.

That's for a year supply.

Hillary: And the process patients, like Gunnar, have to go through to get Trikafta has many steps.

Gunnar: I have to be diagnosed with CF. Then, I need to be genotyped. Then, I need to have liver function monitoring. And then after, that my doctor submits a prior authorization to my insurance company.

The insurance company approves the prior authorization, which is effectively a third party agreement that the drug is appropriate for me. And then finally, a copay is levied against me before I can get the drug from the pharmacy. So I have to go through all these steps to get to the drug.

[MUSIC]

Hillary: Now, before we dive into what goes into the price of a drug, we need to talk about patents. They're basically a territorial right granted by a government to protect an invention for a limited time.

In the U.S., a new drug patent typically lasts 20 years from the application date. And there are many types of patents.

Once the patent expires, other companies can produce cheaper generic versions of the drug.

But generally speaking, drug makers would file for a patent at some point during the drug development cycle—a process that can be very long!

Peter: It takes about 10 years to get through clinical trials and development all that on average.

Hillary: Peter Kolchinsky is a biotechnology investor and a scientist. He's the author of the 2020 book *The Great American Drug Deal: A New Prescription for Innovative and Affordable Medicines*. Peter says that decades ago, Congress recognized that if it takes makers about a decade to develop a drug, that eats up half of the time or more from their patent.

Peter: And they didn't think that was enough. And so, they created a concept called “patent term restoration”, where they said, we will give you back about half the time that you spend in clinical development or regulatory review, like FDA review, up to a maximum of five years and no more than 14 years.

Hillary: That’s the essence of the 1984 Hatch-Waxman Act, which establishes a 14-year average period of price exclusivity for drugs.

Peter: That is about the period of time that I've been calibrated to expect the drug will be on the market before it goes generic as an investor.

Hillary: Peter describes the cost of brand-name drugs as similar to paying off a mortgage. We pay more during the patent period, but once that expires, the drug becomes this low-cost, long-term resource in its generic form, benefiting everyone.

Take Lipitor, for example. When it became available as the generic Atorvastatin, the price dropped from over $5 per pill to less than 20 cents. This made cholesterol treatment much more affordable and saved billions in healthcare costs. In turn, these savings help lower premiums and out-of-pocket expenses for patients.

But there have been some bad actors at play who find ways to game the system. Martin Shkreli is a great example. He's the former CEO of Turing Pharmaceuticals, and he made headlines back in 2015, when he drastically hiked the price of a life-saving drug called Daraprim. This drug, used to treat a parasitic infection, had been affordable for

years, but after Turing acquired it that year, Shkreli raised the price from $13.50 to $750 per pill. That’s a shocking 5,000% increase.

Peter: That was a really old drug. Turing didn't really do anything different to it. They just acquired it for cheap from another company, which acquired it for cheap from another company, and just raised its price.

Hillary: Not every brand name drug in the market has a generic version today, but the idea is that eventually they all will.

Gunnar: What will happen in Trikafta's example is the drug will go generic at some point in the 2030s.

Hillary: Gunnar Esiason again.

Gunnar: There are some extensions or exclusivity centers that exist as incentives from regulators and things like that. But ultimately, Trikafta will go generic, and it will be quite easy actually for generic drug makers to copy Trikafta's chemical structure and then produce equivalent generic medications.

Hillary: Which is fantastic for patients and payers but gives makers and investors a finite runaway to make profit from all the resources poured into development.

Gunnar: Most of the drugs that people take today are actually generic medications of drugs that have been around for a long time, and those drugs are basically pennies on the dollar from where they started years ago.

[MUSIC]

Peter: New drugs that have a high price… that's not a bug. That's a feature of the market. They're supposed to ultimately command a high price.

It's not like you launch a drug, and you're guaranteed commercial success. Plenty of drugs launch, and they either get the pricing wrong or they misjudge what the market need is, and it's a commercial flop.

Hillary: Peter says his journey in this space actually started when he was a teenager, hanging out on the beach with his dad.

Peter: My dad was in the computer hardware field, had actually started up his own business. At one point, he said, my son, I feel like I've caught the computer wave, and it

was the right wave for me, but I think that the right wave for you might be this new emerging field of biotechnology.

Hillary: Coming out of grad school with a PhD in virology, Peter started working for biotech entrepreneur Richard Aldrich. With him, Peter managed cash and stocks and eventually became an investor. That work seeded what today is Boston-based RA Capital Management, and it ignited a curiosity in Peter around what drives costs in this field.

Peter: When a drug is highly in demand, despite its high price, and if it's a new drug, that's a powerful signal to the inventors that they did a good job. But when it's an old drug that has a high price and society keeps paying for it, that's a signal that you have successfully patent gamed or price checked or whatever. And that is only going to encourage more people to try to do it. We don't want to be rewarding that.

[MUSIC]

Hillary: Ok, let's zoom out here. To really grasp how drugs are priced in the United States, it helps to think of the market as an ecosystem. In this ecosystem, drug makers, insurance providers, and a whole bunch of other players are all interacting.

These interactions create a complex system where every part plays a role in keeping things running, well sort of. And the way these interactions play out directly affects how affordable drugs are. So let's start with the makers…

Peter: At any one time, you should try to imagine that there are thousands and thousands of brilliant innovators. These can be scientists in academic laboratories, or they can be scientists who are just free agents, and they have an idea.

Hillary: So, let's pretend I have this amazing idea for a drug to cure asthma. We'll call it AsthmaOne.

Peter: And they say, I think if I can make the following kind of molecule, it will bind to a person's protein in the following way, and it will really meaningfully treat this disease. And I need money to do this. It's going to take you like a decade.

Hillary: So, at this point I need a team and a lot of resources to get my chemical structures right.

Gunnar: There's two distinct parts of drug development.

Hillary: These days, Gunnar Esiason is the head of patient engagement at RA Ventures, the venture incubator at RA Capital Management.

Gunnar: First, there's the work that happens preclinical, and that's sort of all the magic that happens inside the lab, like having a eureka moment.

Hillary: So, I need to run experiments, collect data, test my idea…

Gunnar: And then there's the clinical trial part of it. Both are extremely difficult.

Hillary: Before Trikafta's successful clinical trial, Gunnar went through several clinical trials with other companies that didn't improve his symptoms at all.

Gunnar: I saw the struggle firsthand. I think most people don't actually see the struggle. They only see the outcome.

The clinical trial process is designed by our regulators to make sure that drugs are both safe and effective for different populations at different indications. So there's typically a phase 1, a phase 2, a phase 3 trial, and all of this sort of goes down the development path that our regulators, the FDA or international regulators, will adjudicate.

Hillary: But Gunnar says the infrastructure at this stage can be very fragile. And that's adding to the cost of my AsthmaOne development.

Gunnar: Drug companies are contracting with individual research sites. They're oftentimes outsourcing a lot of their clinical work to big sort of bureaucratic organizations called CROs, contract research organizations, with all sorts of vendors in between, and they have to find the right kind of patient to enroll in the trial to actually test it.

The part that I played was I was a research subject, and I saw it from the inside. I saw how finicky the technology was that was evaluating the medications. Oftentimes, the people that are running the trials are 22, 24 year old employees of these medical systems, and they have very hard administrative jobs. And as a result, the turnover rate is super high. So, there's all these economic issues that sort of feed into the difficulty of clinical trials.

Hillary: At this point you might be wondering, what about the big pharmaceutical companies?

Peter: Pharma is just a bigger version of biotech….

Hillary: Peter Kolchinsky again. Sometimes big pharmaceutical companies like Pfizer for example, have an in-house drug development process, but more often, they just acquire other companies that have already successfully developed a drug or have promising drug candidates in their pipeline.

Peter: A better split would be to think about builders and landlords.

Hillary: Builders focus on creating new drugs and maximizing profits, knowing those profits end once generics hit the market. This is where the mortgage analogy comes in—because after paying off a mortgage, you've paid for what was built, so in order to keep earning, builders must create something new, and in this case, we mean new drugs.

Landlords, on the other hand, focus on making money from older drugs, often using patent loopholes, and this undermines the original purpose of the patent system.

Peter: Pharma has both builders, innovators, and it has landlords working in it. Where small biotech companies are naturally only builders. And so, if you think of the schism in our industry, not as biotech versus pharma, but as builders versus landlords, you'll recognize that big pharma is good too. It innovates too. It has a builder mindset in it. It's just also potentially contaminated by landlord behavior.

Hillary: So, while big pharmaceutical companies do have the potential to innovate—and many do—there's always that tension between developing innovative, impactful drugs and earning the greatest return.

Ok, so back to my AsthmaOne drug journey. After developing it, I need to manufacture enough of it to conduct the clinical trials.

Peter: And the FDA has a high bar for you to prove that your drug is safe and effective. You're going to need a whole team to do this. And where are you going to get that money?

[MUSIC]

Hillary: And here is where we can identify yet another stakeholder in our drug pricing ecosystem: the investors.

Peter: There are certainly wealthy people that invest themselves, those are angels. But most of the money for things like that, are in funds, like mine, that derive their capital from pension funds and university endowments and high-net-worth individuals and

families, but it's basically society's money. Teachers and firefighters through their pension funds are risking their capital on these kinds of projects.

Hillary: RA Capital Management has been investing in drug development, medical devices, and diagnostics for over 20 years, so Peter and his team often receive pitches from scientists and entrepreneurs at this very early stage, looking for the funding they need to bring their ideas to life.

Peter: We may say no, or we may say yes. And if we say no, and if every other investor out there says no, then it's like society's hivemind has ultimately said no to that idea, and it won't come to be. But if even a few neurons of that brain say yes, then that's enough, like you don't need all the investors in the world to say yes to your project. You just need a few. And so, I view our role at RA capital as contributing to that calculus and we want to make the right decision.

Hillary: So, if I'm able to secure funding from investors, I actually have a shot at making my drug work.

Peter: I would say that it takes 100 shots like that in order to end up with maybe 10 drugs that are worth taking into the clinic, of which then over the years, one of them will end up being good enough to get FDA approval.

Peter: So, when you are making that investment in that innovator's idea at that early, early phase, what price do you imagine you would need to charge someday if you're successful in order to make your investment decision rational? You'd better make a boatload of money on the one out of 100 projects that will actually succeed, right?

Hillary: Now, not all investors want to risk capital on preclinical companies. But Peter says that even if you wait and invest later on the cycle, it’s still quite risky.

Peter: If you wait until the drug is on the market, and therefore, you're taking no clinical risk, presumably you're going to be paying a high price for that stock, thereby rewarding everybody who helped create that company. And at that point, that high valuation can only be supported if that company is actually charging high price and is getting reimbursed.

Peter: So, how's that price ever going to be affordable to people?

[MUSIC]

Hillary: Venture Capitalists need to agree with startup founders on the value of a drug in development, which might be the startup's only asset. To do this, they rely on what

are called “valuations”. Companies are often valued through various methods that factor in financial metrics, market trends, and industry expertise–but it’s ultimately a prediction about the company’s future profits.

Dean Dimizas: We want to make sure we're not overpaying for the risk that we assume.

Hillary: Dean Dimizas is a Partner and Managing Director at Cambridge Associates' Boston office.

Dean: For good or for bad, unfortunately, valuation is tied to interest rates. You know, somebody asked me why should interest rates be connected to saving lives, but unfortunately, the nature of the beast is that these companies that we invest in have revenues and profits that are very far out.

Hillary: Meaning, if I'm developing AsthmaOne today, regardless of whether or not it's successful, my funders and I won't see returns or losses for years, and possibly even decades.

Dean: So, this ends up becoming a very interest rate sensitive sector. The cash flows on the revenues down the road will be directly linked to the net prices that these drugs will command in the market. We have to strike the balance between compensating our clients, the family offices, the endowments, and the foundations that are assuming a lot of risk and tying up their capital for many years, which has a huge opportunity cost, while balancing the needs of everybody else in the ecosystem to make sure that patients with unmet needs can get the drugs they need to improve their lives.

Hillary: But striking the right balance between long-term financial success and equitable access to drugs for patients is a challenging task.

Peter: You've got manufacturing expenses, sales and marketing, your drug sales are going to ramp over time.

Hillary: Imagine there are 100,000 people in the U.S living with Huntington’s disease.

Peter: So, if you had a drug that could help all of them, you would probably need to charge somewhere on the order of let's say $100,000, if you wanted that to be a 10 billion a year drug.

Hillary: So, that would be the number of patients -100,000- times the drug price per patient -$100,000- that gets you to that price tag Peter is referencing. And it's set by the pharmaceutical manufacturers.

Peter: And Vertex’s Trikafta is in that range.

If you're gonna invest in a preclinical project for Huntington's, you probably should be aspiring for your drug to make north of a billion dollars per year. And when you look around at other drugs for these kinds of what are called “orphan diseases”, “rare diseases”, charging a hundred thousand dollars is not atypical. And of course, you know, that if you charge a hundred thousand, that's unaffordable to almost anybody.

Hillary: And here a new player enters the ecosystem: the payers!

[MUSIC]

Peter: Nothing in healthcare is affordable without insurance, so you need to count on insurance. Insurance plans do pay that.

Hillary: In the healthcare system, a "payer" is basically anyone covering the cost of your care—it could be a commercial insurer, a health plan provider, or government programs like Medicare and Medicaid. Employers are also big payers. They contribute over $1 trillion dollars to U.S. healthcare, with nearly half of all Americans getting their insurance through their work.

At Cambridge Associates, the company ultimately decides what is covered and at what level. And to make these decisions, our HR team relies heavily on market trends, advice from our benefits broker, and an annual meeting with insurers to review CA’s claim experience.

And as a patient, your insurance can deny coverage for various reasons. Like, they may require you to try less expensive drugs or alternative treatments.

[MUSIC]

If we consider my hypothetical AsthmaOne as an example, we can pinpoint even more stakeholders in the ecosystem. There are the wholesalers who distribute the drug, and the pharmacies they sell them to.

And AsthmaOne may not even be on every insurance company's list of approved drugs.

Peter: You might need to have a free drug program. So, what fraction of that hundred thousand is gonna actually get covered?

if you started thinking like oh no, I bet only 10 percent. That would be a billion dollar drug.

Now I know a billion dollars may seem like a lot, but latest math suggests that to develop one approved drug the industry collectively has to spend somewhere on the order of four or five billion dollars.

Hillary: So, let's imagine that AsthmaOne will be covered for 60% of the eligible population. That's about $6 billion a year that I -and my investors- would get if I sell the drug to all those people in the U.S.

Peter: That's attractive, right? Especially if you can get that for about 14 years and there's a chance you'll make some money off the rest of the world. So maybe the global market ends up being like 7 billion. That is a big jackpot.

What if it turns out that lots of people try to develop a drug and four or five make it across the line at about the same time?

Hillary: Peter says we have to consider price correction here.

Peter: You have to believe that if this problem is so hard that only you will have a chance of solving it. Well then, yeah, you might be able to make 7 billion dollars per year until your drug goes generic.

But if it turns out that the challenge wasn't as hard to solve…

Hillary: Say 4 other makers were able to create something similar to AsthmaOne at about the same time.

Peter: Then society ends up being able to cut back on the reward by making the multiple companies that made it over the line compete against one another, and it sparks a price war through what are called “PBMs”.

Hillary: PBMs are pharmacy benefit managers, and they act like the middlemen between some payers -so think insurers, employers, and government agencies- and pharmaceutical companies. They determine things like copays.

And while a PBMs goal is to lower drug costs, sometimes they prefer that you take brand name rather than generic drugs because they can ultimately get more money in the form of rebates.

Peter: Right now, everybody's hating on them and saying that they're evil, and they charge patients too much money and all that, which is, by the way, all true, except PBMs also provide an important service to society. They are a vital part of keeping this market thriving. If I'm going to fund a company that is, maybe the second or third or

fourth to market, I want to know that if my company offers a lower price, we will win some market share. That's a PBM that makes that happen.

Hillary: But Gunnar says that to capture the real value a drug holds for society, you need to see the big picture.

Gunnar: If you look at a drug like Trikafta, over call it a hundred year time horizon so, from the day it was approved by the FDA and the end of 2019 through 2119, You can see how the cost of cystic fibrosis will basically go down to nothing once the drug becomes generic.

Hillary: Although Trikafta commands a high list price, today, the system here in the U.S. has made it available and affordable to eligible patients.

Gunnar: For the most part, people with CF, me included, are paying somewhere between 15, 30, dollars, if you're well insured.

Hillary: But that's not the case for every drug in the market, and it is certainly very different from what happens overseas.

[MUSIC]

> **BBC News video:** *A new treatment for cystic fibrosis, described as "truly life changing", is being made available for NHS patients in England.*

Hillary: This is the BBC News in July of 2020, just a month before Kaftrio -as Trikafta is known in Europe-, was first made available to UK patients.

> **BBC News video:** *Experts say that 9 out of 10 people with the life limiting condition will benefit from a three drug combination.*

Hillary: But in November 2023, the UK's National Institute for Health and Care Excellence, NICE, said the drug was probably too expensive to be worth the cost for the National Health Service.

In a country with just one national healthcare plan, a decision like that can effectively block access to costly, yet life-changing drugs. In the end, NICE gave the green light in July, allowing the drug to be used across the NHS in England, Wales, Scotland, and Northern Ireland but only after more negotiations with Vertex.

Peter: They ultimately capitulate and just say, look, making some money from these countries is better than making no money.

Hillary: Vertex Pharmaceuticals has been guarding the drug under strict patent laws, but that’s now being challenged. Under international agreements, there are ways to ensure people can access life-saving drugs, even when patents are in place. In South Africa, for example, legal papers were filed to allow more affordable generic versions of the drug. Other countries, like the Netherlands and Canada, are also pushing for big price cuts. They argue that Vertex's pricing is just too high.

Peter: You wouldn't want to not sell a drug in the rest of the world. But they are mostly free riding off of innovation that is incentivized mostly by the American market.

Hillary: Peter estimates that around 80% of a drug's profits come from U.S. sales, with just 20% coming from the rest of the world.

Peter: It's actually not that different from global defense. America spends a fair bit on its military. Our Navy patrols the world's oceans, and we keep telling other countries, like we'd really like you to spend more on your militaries. If the US ever cut back on its military spending, well the US would be less secure. You know, there’d be more piracy on the open seas. The cost of commerce would be higher. We'd be paying more for our goods.

Peter: Well, similarly, when we invent drugs, we're inventing drugs for American patients. And it's nice that we can also help all those other patients in the rest of the world, too. There's some marginal profit from it, as well. But America should not make the mistake of thinking that it can pay as little as the free riders. You gotta spend what it takes to come up with these kinds of innovations in order to make all our lives better.

Hillary: Peter says we should push other countries to pay their fair share, and that's better achieved through trade policy. But it's actually internal policy that's making the rounds these days.

> **Biden 2024 State of the Union video:** *Americans pay more for prescription drugs than anywhere in the world. It's wrong, and I'm ending it.*

Hillary: In his State of the Union address in March 2024, President Joe Biden promised to protect and expand the savings from the Affordable Care Act and to push for Medicare to negotiate prices on more prescription drugs.

> ***Biden 2024 State of the Union video:*** *Instead of paying 400 dollars a month or thereabouts for insulin with diabetes, it only cost 10 bucks to make. They only get paid 35 a month now and still make a healthy profit.*

Hillary: This echoes parts of the Inflation Reduction Act that President Biden signed into law in 2022. The IRA included provisions to lower prescription drug costs for Medicare users and reduce drug spending by the federal government.

Peter: The trouble I'd say in biotech and the biopharma space is that I think that we as an industry, we're so focused on innovation, we forgot that we are there to serve society's interest to ultimately build up its generic armamentarium.

Hillary: In his book, *The Great American Drug Deal*, Peter argues that legislation could be a game changer to make drugs more affordable.

Peter: If you can pass a law that guarantees that all drugs will have to abide by the intent of the patent system, and go generic without undue delay, then it eliminates the landlord behavior. So essentially what that law would look like is if your drug hasn't gone generic by a certain year…

Hillary: In his book he proposes 15 years.

Peter: …then we just price control your drug down to roughly two times the cost of production because two times the cost of goods is about where all generic drugs price. It's what competition would have done to your drug if it could set in, but since competition is not working to lower the price of your drug, we'll just fix that market failure with a regulation.

Hillary: In the book Peter calls this a “contractual genericization”.

Peter: The interesting thing is that this IRA bill actually have that. They didn't set 15 years. They set 13 years. But sadly, they only applied that to a subclass of drugs called “biologics”.

Hillary: These are a variety of drugs made from living organisms or their byproducts.

Peter: So, they got that right, and they also lowered out of pocket costs for Americans. They set 2,000 dollar caps. Now the bill only applies to Medicare. So eventually I hope caps like that are spread across all insurance plans, so all Americans get that protection.

The trouble is that that bill went a step too far for small molecule drugs.

Hillary: Those are all the drugs you take in pill form.

Peter: They said, by the way, we get to price control all small molecule drugs that haven't gone generic by nine years after launch. Like no small molecules go generic merely nine years after launch, and what that's done is made small molecule drugs for Medicare covered disease, which means diseases of aging, people who are older: cancer, Alzheimer's, things like that. It's made the early stage investing there irrational. Like the mortgage period is just too short.

Now you may think, why don't you just charge more for merely nine years? Well, the trouble is that insurance companies, if they think your price is too high, they won't cover a drug. So, you can't just assume that you can charge whatever price you want, you know, to make your own investing math work, just because Congress shortened the mortgage.

Hillary: Peter explains that while this helps some in the ecosystem, it doesn't help everyone. For pharma companies, they'll have to take a hit on some drugs that are currently mid-patent. They expected these drugs to bring in returns for 14 years, but now they'll only have 9 years to do it.

Peter: But it's not like the houses are going to be unbuilt. The houses were already built.

Hillary: Meaning the drugs are already in the market.

Peter: So, no damage done, just somebody got seriously disappointed about you know, how much money they're now not going to make.

Hillary: The problem is that this might hinder innovation. If we follow the mortgage analogy, Peter says that the point of a 30-year mortgage is to reduce premiums to make a house affordable. So, if you shorten that timeframe, houses actually become less affordable because the cost of building the house remains the same, but now it has to be paid in less time.

Peter: So, if Congress keeps shortening that period, then you're just making these medicines uninventable.

Hillary: And in a fast-changing industry, many people argue that innovation can effectively help to lower drug prices.

Dean: I think innovation will create new drugs that can be cheaper in some cases. New drugs that may come to market may have different mechanisms of action.

Hillary: Cambridge Associates' Dean Dimizas.

Dean: For example, in one of our last episodes, we talked about the GLP drugs.

Hillary: He’s talking about episode four from last season about the future of obesity therapeutics.

Dean: As everybody knows, these drugs for obesity now are for the most part injectable form, but newer versions of these drugs over the next few years could be in a pill form that would dramatically decrease the cost of production, the net price for these drugs, which would improve affordability and increase access.

Hillary: Improving effectiveness in clinical trials or streamlining prior authorization can also have a positive impact on prices.

Peter: We need truth in insurance, which means low out of pocket caps on all plans. We need to make sure that all drugs go generic without undue delay, which means that we do need some price controls as a backstop in case a drug fails to go generic.

Dean: I think there's often a lot of confusion in terms of which part of the ecosystem is “guilty” for high drug prices. It's easy to point to the companies themselves, but the whole food chain is quite complicated.

Hillary: And Dean says that funding drug companies is both an integral part of life sciences investing, as well as an opportunity to affect real change.

Dean: We have to strike the balance between incentivizing the investors in this space. Our clients are assuming a lot of risk to tie up their capital for 10, 15 years for early-stage life science investing. So, they have to earn a very attractive return so they can continue doing it. But at the same time, we have to be mindful that drug pricing is very related to access, and we want to make sure that these drugs will go into the hands of the patients globally that need them.

I'm very excited with every incremental dollar that we can put into this space that whether it's cancer, whether it's an autoimmune disease, whether it's a neurological disease, whether it's something else, we'll have solutions in a few years, solutions that we don't have access to them today. So, we're very thrilled with the positive impact of investing in this space that our clients have been funding.

Peter: My hope would be that ultimately all investors see the totality of this ecosystem and how various policies impact innovation.

Hillary: Peter Kolchinsky again.

Peter: And I know that investors aren't just investors they're also human beings. We all have a personal stake in getting this right. Congress does need to hear from investors. It shouldn't just be guessing as to how we act.

Hillary: Making drugs truly affordable means rebalancing the entire ecosystem, and in this episode we barely scratched the surface! The system is complex, and that complexity is a big part of why drug prices have gotten so high. And while it's far from perfect, the system has benefited many people.

Gunnar: The system was already paying for my cystic fibrosis before Trikafta came out, I was a super utilizer. These things are massively costly and like that's all just gone away at this point. I was very much a taker, now I'm very much a giver.

Hillary: Gunnar's experience motivated him to work in this industry, and he's now focused on making a difference in other people's lives.

Gunnar: We are at the very tip of the spear when it comes to seeing patients receiving super innovative medications that can hopefully treat them and improve their conditions.

The feeling that I get when I leave the office is like intense optimism because I get to talk about 15 different diseases in a single day, but all 15 of those diseases might have a candidate in the pipeline that we feel super excited about. So, I think venture capital really does support the future of what the drug industry can and should look like.

Hillary: If you want to learn more, please visit us at cambridgeassociates.com/unseenupside or check out the show notes. If you like what you're hearing, leave us a review and tell your friends and colleagues.

At Cambridge Associates, our podcast team includes Michelle Phan, Megan Morrissey, and me, Hillary Ribaudo. And a special thank you to Robert Scherzer, Krista Matthews, Song Han, and Christian Rolleau.

From PRX Productions, Sandra Lopez-Monsalve is our producer, with support from Isabel Hibbard and Emmanuel Desarme. Genevieve Sponsler is our editor.

This episode was mixed by Samantha Gattsek. The executive producer of PRX Productions is Jocelyn Gonzales.

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