

"Eli's Gift"

DRAFT

By Nate Binzen

Characters:

- Dr. Raymond Ferris, director, Human Gene Therapy Center, Franklin University, Philadelphia
- Eli Schroeder, 18-year-old patient who dies in gene therapy trial
- Hugh Schroeder, Eli's father
- Angie, nurse at Franklin University Medical Center
- An inner voice speaking to Eli
- Dr. Sarah Moore, president of Franklin University
- Dr. Carla Zetta, FDA regulator
- Dr. Andrew Ireland, gene therapy pioneer and booster
- Dr. Van Desai, president, American Society of Gene Therapy
- Patients' advocates
- Dr. Robert Virden, Franklin University Medical School Senior Vice Dean
- President Clinton

To be staged in *presentational style*: stage with no set, and the company of actors can play multiple roles. Scenes present a flow of events over the course of one year, rarely featuring dialogue between two or more characters.

Note: (p) indicates passages that include direct quotes from the public record.

ACT I

Scene 1. A hospital room in Tucson, Arizona, WA, early 1999

Eli sitting up in his hospital bed, Hugh visiting

HUGH

Eli, how ya doing today? The doc says you're a whole lot better.

ELI

Yeah, I feel better, but... I don't know.

HUGH

Whaddaya mean?

ELI

This is just so stupid. I mean, one minute I'm shooting hoops, next minute I'm laid up on the ground, and next thing, I'm waking up in the hospital. I can't believe I have to live this way.

HUGH

Well, we've talked a lot about the diet and the drugs, the docs and me, and I really think this doesn't have to happen again. We've got ways to get your OTC pretty much totally under control.

ELI

Great. I gotta watch everything I eat, I gotta take drugs every day for the rest of my life.

HUGH

Eli, hey, it's not such a bad deal to live a normal life!

ELI

Why me? No one else I know has to go through this crap.

HUGH

E – I know it's tough. But believe me, there's a lot of things in life that can make you a whole lot more miserable. Your disease is manageable, and that's what we're gonna do.

ELI

Well, I'm pissed off. It's not fair.

Scene 2. Gene therapy conference, Seattle, WA 1997

Ferris at the podium, speaking to a public audience

FERRIS

Good afternoon. It pleases me to be able to report to this conference on recent developments in gene therapy. Gene therapy will revolutionize the way we think about sickness and health. Through gene replacement – substituting sick genes with healthy ones in a person's body – we will alleviate suffering in ways that no one had thought possible. By attacking disease at the source – at the level of the genes that cause disease, we'll go beyond medicine as treatment to medicine as prevention. We want to develop a technique that is both much more powerful, and far less invasive, than conventional measures.

As director of the Human Gene Therapy Center at Franklin University, the job that I'm doing is my highest calling. Have you ever seen a baby die from an inherited disease, before that child ever had a chance to grow? Have you talked to the parents of an infant who cannot live? Because I have. That's why I got into this new science of genomics. I was tired of the powerlessness I sometimes felt in the face of such tragedies – I was sickened by it.

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When I began human gene experiments back in 1992, we wanted to treat a rare liver disorder called familial hypercholesterolemia. We had to remove liver cells from the patient's body and then, in the lab, infuse those cells with our retroviral vectors. Then we would return those cells, with their new genes, to the patient's liver. We demonstrated that gene therapy conducted *ex vivo* – outside of the body – could work in humans.

But that's really not good enough. What I realized was, this therapy will not have any medical relevance until it has commercial viability. That means we need to develop what I call "injectable genes." Ordinary doctors and nurses must be able to take a bottle of genetic treatment off the shelf, and administer it into the patient's body with shots. That's what I've been working since then.

My friends, it gives me great pleasure to announce today that the National Institutes of Health have approved our latest gene therapy trial: the subjects in this trial have the gene for *orthinine transcarbamylase* deficiency – we call it OTC deficiency. OTC is a rare hereditary disorder in which the liver is unable to process ammonia. Now, ammonia is commonplace in the body – it's a toxic byproduct of protein – and the liver's job is to break ammonia down. If the liver fails to dispose of the ammonia, the ammonia builds up in the blood, and it can travel to the brain, causing coma, brain damage and death.

That's why OTC can be fatal – and most often is fatal in infancy. It's to save the lives of infants that we're trying to develop a genetic treatment for OTC. Now, I want to tell you a little bit about the care we have to take in selecting and working with subjects in gene therapy trials. The NIH's oversight committee for gene therapy, the Recombinant DNA Advisory Committee – we call it the RAC (pronounced "rack") – has decided that, for ethical reasons, we cannot conduct tests on critically ill infants. So instead, we are selecting from adult subjects with a milder form of OTC, who have the disorder fairly well under control.

We are working towards the day when OTC and many other disorders are fully treatable, even preventable, by genetic replacement therapies. My conversations with parents and sufferers of OTC and other disorders have convinced me time and again how terrible is our need for the benefits of this research – and I'm confident that those benefits are coming soon.

Scene 3. Schroeder home, Tucson, AZ August, 1999

Eli and Hugh

(both speaking the medical terms tentatively)

HUGH

Okay, let's get everything clear before our conference call on the consent forms. This is a big decision for a guy who's only just turned eighteen.

ELI

Alright, let's go over it.

HUGH

So they put the modified OTC gene in a cold virus.

ELI

(reading) "an inactivated, um, adeno-... *adenovirus*, to carry the new corrective gene to the targeted cells."

HUGH

That's what they inject.

ELI

A ton of 'em. Like they said, they use the cold virus because people get exposed to it all the time, and nobody ever dies from it, they just get a cold at worst.

HUGH

So inject them into the... (reading) "hepatic artery, which leads directly to the liver."

ELI

Then it goes to work. And maybe I get a cold.

HUGH

"Slight flu symptoms" for a couple days.

ELI

Yeah, cuz the body is already so used to them, they're a good bet.

HUGH

Unbelievable. Imagine switching the genes in and out of a virus! Making a bad virus into a good one! Someone oughta do that with computer viruses.

ELI

Really.

HUGH

That's what they call the *vector*, the thing they use to bring the DNA into the body. They said they've already used adenovirus in about 70 other studies so far.

ELI

And it says on the consent form, they did a bunch of experiments on mice, a bunch on monkeys, and they've already given this to seventeen other human patients. They say it's totally safe.

HUGH

Either the stuff takes hold, or it doesn't work and nothing happens.

ELI

Are we all set?

HUGH

Yeah, I am. I'm really glad you're doing it.

ELI

Thanks.

HUGH

I'm proud of you. I mean, you're not even doing this for yourself.

ELI

It's what I realized after that coma a couple months back – OTC is a life sentence for me. The diet and drugs, I can keep it from happening again, but it's not ever gonna get really fixed. But if I can help someone else be free from OTC, why not?

HUGH

Very noble. Helping babies who haven't even been born yet. I just hope it helps them find a cure.

ELI

Yeah, it'll be worth it.

HUGH

I just wonder about sending you there on your own. You've hardly ever been outside of Arizona!

ELI

Well, I'm all right.

HUGH

Okay, they'll be calling in about ten minutes....

Scene 4. At the Human Gene Therapy Center, Franklin University, Philadelphia, PA, August, 1999

FERRIS

(on the phone with a nonpresent colleague or business partner)

Well, yeah, of course there could be a lot of money in this if things go our way. But really what I'm doing this for is to heal, that's the bottom line.

(pause, listens to caller)

That, and pushing the limits of what medicine can do in order to heal.

(pause, listens to caller)

I get a charge from being out in front, sure. It's like my dream job. It really makes me feel good.

(pause, listens to caller)

Well, we're sharing the patents – the university and my company.

(pause, listens to caller)

Uh-huh, that's the way this field is working now, public-private partnerships, investment mixes between universities and biotech firms.

(pause, listens to caller)

Genetics? I started Genotics a couple years back. The idea was, we could get our own financing, as well as what we get from the university and the feds.

(pause, listens to caller)

Actually, it's no picnic, we're under a lot of pressure now. You know the stuff in the press – “gene therapy has long fallen short of its promise. Almost 300 trials and nothing's been approved or gone to market.” ... Yeah, All that stuff.

(pause, listens to caller)

Not only do we need to maintain the public's belief that we're getting somewhere, to keep the federal funding flowing, we've also got investor expectations riding on our backs.

(pause, listens to caller)

Yeah, we could have something really huge here! When this stuff starts to work, which'll be soon, I really think so...

(pause, listens to caller)

That's the thing, it's gonna go way beyond just OTC. Commercially, the key is to get the vector right. See, if we can apply this vehicle we're using to deliver the genes – adenovirus – to a lot of other genetic diseases, and we can license that method – well....

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(pause, listens to caller)

Well, the thing about the feds is, you see, the RAC, the Recombinant DNA Advisory Committee, everything that goes through the RAC is for public disclosure.

(pause, listens to caller)

You should talk to some of my fellow researchers about “adverse reaction reports.” When we report to the feds in detail on every little adverse thing that happens, that info goes straight to our competitors. So who finds out everything we’re doing?

(pause, listens to caller)

Uh huh, and Genzyme, Genentech, Merck – they’ve all got our latest data the very next day cuz of the public process!

(pause, listens to caller)

Yeah, it is. But you know what? I think we all know we’re playing a game right now. I mean, the RAC, the Congress, the president, they all want to get a breakthrough to commercial viability. I mean, the RAC isn’t going to rain on our parade. I think it’s more like “don’t ask, don’t tell” right now – the way I see it, they’re operating on a “need-to-know” basis! Really. At least that’s the idea I get when I talk to other researchers.

Scene 5. Franklin University Hospital, Philadelphia, PA, Sept. 13-17, 1999

ELI

Nurse, I don’t feel right – I am so overheated. What’s the story?

NURSE

Well, you are running a very high fever, Eli.

ELI

I feel really bad.

NURSE

We’re going to do what we can to bring the fever down.

ELI

But is something going wrong? You know, my body can’t handle too much like this...

NURSE

This isn’t so abnormal, Eli...

ELI

Yeah, but I had a coma a while back... That could happen again.

NURSE

Eli, you're going to be okay. I'll be back with you in just a little bit.

(Nurse exits to another room)

NURSE

(on the phone to Dr. Ferris)

Dr. Ferris? This is Angie at the Medical Center. Eli Schroeder, the patient who got the gene vector this morning? I think you better come down here. He has spiked a very high fever – higher than you would like – he's over a hundred and three point five.

(pause, listens)

He looks jaundiced. The most recent blood draw showed that his LFTs were *really* abnormal. Do you think he may be showing signs of hepatitis or liver failure from the vector? He's really uneasy about it.

(some time passes here)

ELI

(glazed, sounding goofy or drunk)

"How am I doing?" I...uh...really bad... It kills... What's going on? ...I...uh... not gonna give me another coma, is it?... I ... wanna...

DR FERRIS

OK, Eli, don't worry. Your lab tests *are* abnormal and your liver appears to be having a reaction to the vector. But we're giving you some drugs that should cool the fever and take the stress off your liver.

(some time passes here)

NURSE

(on the phone to Dr. Ferris)

Dr. Ferris? His temperature is now a hundred and four point five. He's been getting worse every hour. He's coagulopathic, and his ammonia's rising fast. If we can't stop this liver failure, he's going to go into a coma. How do you think the vector could be complicating this?

(some time passes here)

DR FERRIS

(on the phone to Hugh Schroeder)

Hello, Mr. Schroeder? This is Dr. Ferris, at Franklin. I'm calling about Eli. He's had a bad reaction to the drugs... I think you perhaps ought to come up here.

(pause, listening)

(continued next page)

We're doing all we can at this time. He's currently stable....but could get much worse very rapidly....

(pause, listening)

Well, he has very high ammonia levels which indicate that his liver is failing. I'm concerned he may become more confused and become comatose from the liver failure.

(pause, listening)

Yes, we'll fly you up here as soon as you can come. I'm going to give you the number of our travel agent, she'll take care of all the details for you...

(some time passes here)

ELI

(confused, slurred)

You got something? ... I've never felt so... uh ... don't wanna go to.... I'm, uhh...I guess I'll see my parents tomorrow.

(passes out into a coma)

VOICE IN ELI'S HEAD

Remember, Eli? You were riding that great stretch of singletrack in the Saguaro National Monument. The ground gave way, your bike sailed out behind you, and you were flying, running in midair. That moment, it went on forever - it was almost funny, remember? – you were a superhero. You could see the pain coming, no telling how bad it would be – and then you hit the ground, you rolled over and over. Remember? Then you were still. And when you stood up, you were alright. You found that out. You were alright.

(pause; then intoning)

Brutal death, my life –
encased in you.
Shudder, how near you are –
still I am untouched.
O Presence, under you –
I am
not obliterated in my very breath –
nor deprived of my inside –
I regard you.

(pause, then conversational)

Jess, you're flying now. You're going to be alright. You're a superhero.

NURSE

(whispering to a colleague)

He's been in a coma since last night, and he's on a respirator; his ammonia levels dropped during the night...but in the last three hours, they've gone through the roof. And it's not just liver failure now – he's septic

(pause, listening)

We don't have a source of the infection, and it's causing him trouble oxygenating on the ventilator.

(pause, listening)

This could be multi-organ system failure at its worst – we're already seeing trouble in his kidneys and lungs. The damage is spreading so fast, he's circling the drain.

DR FERRIS

(to Hugh)

Hugh, I'm sorry.... It's been several days now. We cannot control the wide spread of the infection. Eli's organs have all failed. (deep breath) His liver failure is not compatible with him surviving. In addition, his brain appears to lack any signs of functioning. Initially I wasn't sure why this was... it may have been the liver failure and infection or it may have been that he had some form of brain injury from lack of oxygenation...

(pause, listening)

Well, it has been difficult for us to breathe him on the ventilator.... Hugh, we've gotten the neurological tests, and they do confirm that he has suffered a severe brain injury. (pause) The family may wish for us to continue care, but I feel that at this time there is no meaningful chance of recovery. (pause)

Well, if you wish, we could withdraw support and let nature take its course.... of course, we will make sure he is comfortable – although he is not responding to any painful stimuli at this time. Essentially, then, what will happen is, he will pass away in a few minutes from acute respiratory distress. I'm so sorry. I wish there was more I could do, more I could say....

(pause, listening)

We never expected anything like this. Never in my professional career have I *ever* faced a shock like this. I'm just not sure what went wrong. The blessing, though, is that since Thursday, he's felt nothing.

(in another place)

ELI

(inner voice)

Eli, there's no going back now. It's like you said, I'm crossing the threshold, it's okay. I feel it, I'm going out. Say goodbye. You're gone. Leave my remains to science, doc. It's all good.

VOICE IN ELI'S HEAD

(intoning)

Here is where the light entered
and gave me life.
Where I was left to sway
in the earthly tides,
where I was begun, spun perfect,
where I unraveled in the turbulence of time.

A dream we dream
is this life.
April winds bustling,
leaves bursting,
catkins scattering –
the dream escapes,
dies in a moment's breath –
all is left behind.
No matter, no you,
the blood's fire released.

Scene 6. Hugh by himself, Sept. 18, 1999

HUGH

(to himself)

How could I have let him come here on his own? He was just 18, he wasn't ready to take on this decision – how did I let him do it? Stupid!

ELI

(speaking from beyond the grave, unheard by Hugh)

Whoah, Dad! Check this out. Remember how angry I was? When I had that coma? And then when Doc Ferris came along a few months later? I suddenly saw, for the first time, a way to make sense of my disease – a way to make it right.

HUGH

(heavy sigh)

But I read everything Ferris sent to us with the consent forms. It said, nothing like this has ever happened, in all the animal studies, and in all the people who came before Eli! What was different about him? (pause) A lot of things, I guess.

ELI

I remember those days – see, I felt alive like I never had before. I was saying to myself, it's no longer just me against the world. It's me, part of something bigger, and all those other people around me, and babies not yet born, and maybe someday the kids I'd have. I'm helping them in a way no one else can.

HUGH

Oh, Eli, forgive me...I don't know what I've done, you should never have come here.

God, how could you have let this happen? I pray to you now – give Eli peace. Nobody ever gave themselves like he did. He's a saint – for giving away his life like he did.

I pray those folks at Franklin get the cure they're looking for from this gene stuff – at least that would give Eli a reason for sacrificing his life...

God, you've given me a tragedy – Eli's gone and I'm still here. *Everyone* went into this thing just to help out others, and we've all ended up damaged. God, you shouldn't let that happen.

ELI

Dad, it's okay. Actually, I've never been better! And hear this, Dad: you're okay. You did everything right. Now you're the one who's going on a journey. There's a lot ahead of you that you haven't figured out yet. But you will.

ACT II

Scene 1. At the office of Franklin University president Jean Moore, Sept, 18, 1999

FERRIS (p)

OK, Jean, here's the statement so far:

"We are deeply saddened and surprised by the death of Eli Schroeder, an energetic and bright young man who unselfishly participated in this important study so that, in the long-term, an effective therapy might be developed to prevent or treat OTC deficiency. We offer our heartfelt condolences and sympathy to Eli's family and friends; and we join them in recognizing and honoring the bravery and altruism of this young man in choosing to help advance our knowledge of genetic disease by participating in this trial. We are all devastated by this. Eli truly was a hero in advancing the cause of science."

MOORE (p)

That sounds good. There's something I want you to add:

"The OTC clinical trial has been voluntarily halted until the cause or causes of Eli's Schroeder's death can be determined."

FERRIS

I figured that was coming.

MOORE

Well, don't expect it to turn around anytime soon. The media storm's coming, Raymond.

FERRIS

Don't I know it.

MOORE

It's not going to go away for a while, either. So. I need a complete explanation from you on what went wrong; I need to know everything, Raymond.

FERRIS

Jean, everything's in order.

MOORE

Are you sure? Is there anything I need to know about, right now? Anything you could be liable for?

FERRIS

This was an accident we couldn't anticipate. We followed the regulations, we followed our best medical understanding. We just couldn't see it coming.

MOORE

If we're going to have the lawyers crawling around here, I want to be ready.

FERRIS

What's really worrying me is the damage it could do to the Medical School's reputation. And to the industry. We've got to turn this our way as much as we can, however we can.

MOORE

That's a tall order. Now what are the federal agencies involved in this, and what will they want from you?

FERRIS

There's a group at the National Institutes of Health, it's called the "rack" – the Recombinant-DNA Advisory Committee. They work together with the FDA. They've been responsible for oversight of all gene therapy trials. We have to pass all our plans with them and report to them regularly, especially on adverse events, which this obviously is. I've already talked to them. They'll be checking everything out, and hopefully they'll see it for what it is, a tragedy that was totally unforeseeable. They've got a meeting in Washington coming up in a couple of months, in December, they're gonna be all over this... Also, the FDA is going to do an investigation.

MOORE

(sarcastically)

Great.... If they're gonna do one, we've gonna do one. Look at everything. Find out everything.

Scene 2. A phone call, Philadelphia to Tucson

FERRIS

Hi Raymond, what's up?

FERRIS

(on the phone)

Hugh, I wanted to let you know the results of our latest study. This is very preliminary, of course, and we'll see what others come up with at the RAC meeting in December.

FERRIS

Tell me what you've got.

FERRIS

It seems like patients who receive adenovirus tolerate it well up to a certain point, but once the dosage passes a certain threshold, the side effects become dramatic. We knew that, and we'd seen a gradual escalation of side effects through the three patient groups, as each received a higher dose than the last – but we didn't expect that critical threshold to occur until a much higher level. What happened to Eli suggests that the curve follows an elbow-shaped path, and we just didn't realize it.

HUGH

Well, I know you guys are doing your best to figure this out, and I appreciate it.

FERRIS

I hope what we find out will bring you some peace.

FERRIS

For us, this pain of this thing is still going on every day, but we've gotten a lot of support here.

FERRIS

Good.

FERRIS

What helps me most is knowing that Eli contributed to finding the cure to OTC. And I need you to keep going to make that happen.

FERRIS

It's really important that we *do* figure this out and that we can find a way to learn from it fast. You've heard about the other studies the FDA's put on hold because of this. That's obviously the right thing to do, but we need to learn and start again with something better, because it's so important to maintain folks' confidence that we're finding a better way. We'll never get to the OTC cure if the bottom drops out. Look, I'll see you at the conference in Washington.

ELI

(speaking unheard)

Hu-u-ugh... Do-o-oc... Eli here... That's not all that's on your mind, is it, doc? But we'll all find out soon enough. Dad – I wish you could hear me, but maybe you'll pick up something. You're not totally wrong.

Scene 2. Meeting of the National Institutes of Health (NIH)'s Recombinant DNA Advisory Committee (RAC), Washington, DC, Dec 8, 1999

DR. CARLA ZETTA, FDA REGULATOR

(speaking to the committee)

Thank you, Mr. Chairman. It pleases me to come before the Recombinant DNA Advisory Committee; but it distresses me to bring you the findings that I have on this day. The preliminary findings by the Food and Drug Administration are troubling. I will review the main points now, and return to each of them in more detail later.

The first conclusion that we have drawn is that Eli Schroeder was ineligible for the clinical trial and should not have been treated, because his liver was not functioning well enough at the time of his genetic infusion. His ammonia levels were above those allowed in the protocol. Schroeder had met the criteria at the time he was enrolled – two months before treatment – but he failed them at the time of his treatment.

Secondly, we have found that the Franklin researchers violated our reporting requirements in this trial. They failed to report, immediately to FDA, information about two prior patients in the OTC trial who had also experienced serious side effects from the same treatment. As a consequence, FDA was operating somewhat in the dark at the time of Mr. Schroeder's treatment.

Third: the informed-consent form which was provided to Mr. Schroeder and his family deviated from the one which the FDA had approved. Specifically, this later, modified version of the informed-consent form omitted information about the deaths of monkeys that had received a treatment similar to that given to Mr. Schroeder, albeit in much higher doses.

We do not yet know what the impact of these deviations are on Eli Schroeder's death. But they are important, and when the FDA concludes its inquiry, we will take appropriate action.

FERRIS (p)

(defiant, speaking to the committee)

I must first say how saddened and deeply sorry I am about Eli's death. For the past three months, about one-third of the Center's staff of 250 has been singularly focused on understanding what led to this serious adverse event. I apologize for the fact that there were lapses in our procedures, as I have discovered. I do not believe, though, that these lapses contributed in any way to Eli's unfortunate, tragic death. Sometimes in medicine, things happen that are entirely unanticipated. At no time during or prior to this trial did we in any way expect to see what we saw in Eli Schroeder. There was no prior evidence from either animal or human testing that could have foretold his death. We remain fully comfortable with the clinical decision we made.

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As to the particulars raised by the FDA, we will have to respond to each of them in due course, after we have had time to examine them in detail. But I want to say at the outset that I strongly object to the way in which these preliminary findings were put forward by the FDA today, because in no way are they related to the death of Eli Schroeder; I want that to be absolutely clear. And I am confident that further investigation will show that much of what has been said here is groundless.

HUGH SCHROEDER (p)

(speaking to the committee; "his voice quivering but his composure intact.")

Members of the Recombinant DNA Advisory Committee, thank you. It grieves me to be here today. I want you to know some things about the motivations of the people involved in this sad tragedy for my family.

I'd like to ask everybody to take a quarter out of your pocket, if you've got one...

(waits)

Take a look at what it says. On one side, it says "In God we trust" and "Liberty." You don't see those qualities too much in government anymore. But Eli, he understood freedom. He understood his freedom to choose, and he trusted – he knew – that he'd made the right choice.

Now look at the other side of your quarter. There it says "E Pluribus Unum." I want you to know that everyone participating in this trial demonstrated "E Pluribus Unum" – one for all and all for one. My son Eli set aside his personal life to participate in this trial, he took an unpaid leave of absence from his job. Even though it was not intended to benefit him but rather babies with a fatal form of his disorder.

These researchers have wracked their brains in the past three months, trying to understand what went wrong, and why. I plead with you, researchers and regulators, to keep working together on this. Now is a time for finding the answers and learning from them. You must continue to work together to make this happen.

All these people who participated in this trial did a wonderful thing. They came in with the same intent my son had. It doesn't get any purer.

ELI

(speaking unheard)

Hugh, you're gonna start learning fast. As soon as you figure out you haven't gotten the whole story. That'll be about, oh, about twelve hours from now! These guys have had you in their grip up til now, but they're gonna get what's coming to them. You haven't seen the last of Washington DC.

DR ANDREW IRELAND (p)

(speaking to the committee)

I want to conclude this meeting with a couple of comments. As you know, I've been working with these same issues since before even Raymond Ferris. First of all, we must recognize that cutting-edge medical research is risky. It's unavoidable. If you look at the field of medicine, you realize that, when trying to develop treatments for deadly diseases like heart disease and cancer, bad things happen. People die. They are in a fragile state of life.

You must understand that Dr. Raymond Ferris and his colleagues at Franklin University are outstanding clinical investigators with a long history of the highest ethical standards. If mistakes were made in this trial, they were honest mistakes made by compassionate physicians trying desperately to help their patients.

And I must say especially, concerning this tragedy, that Mr. Eli Schroeder is a hero who gave his life for a cause in which he believed deeply. The development of gene therapy technology is a hope that Eli Schroeder believed passionately in because he knew, he lived out that need. It is a hope that patients who are critically ill from cancer, heart disease, AIDS, and genetic diseases carry with them every day. I know. Like many of you in this room, I have treated and spoken to countless such patients.

I would finish by saying that gene therapy research should not be slowed or stopped as a result of this tragedy. Investigators need to go back to their protocols and make sure that they are as carefully crafted and carried out for the safety of subjects as possible.

Scene 3. At Franklin

MOORE (p)

(making a public statement)

Following the death of Eli Schroeder, we have redoubled our efforts to review all aspects of our research involving humans. I have charged a committee of distinguished Franklin research scientists to take a hard, critical look at our work with human subjects across the board.

I also charged an independent committee of eminent scientists who have no affiliation with Franklin to investigate the Center for Human Gene Therapy's monitoring and oversight of all clinical trials, including the OTC trial in which Eli Schroeder died.

Franklin will take all necessary measures to ensure that our Center for Human Gene Therapy meets the highest possible standards for safety, accountability, conduct and informed consent in all its clinical trials.

Franklin is committed to continuing to conduct research. In that light, we will learn from a death while we continue to mourn it.

Scene 4. Schroeder home

HUGH

(talking to an unseen buddy)

It's unbelievable – check this out. I got a call to testify at the Senate Subcommittee on Public Health. Can you believe that?

(pause, listening)

What else am I supposed to think? Everything's changed. Those guys let me go up there and defend them, and then the FDA tells me that the consent forms didn't even mention that monkeys had died receiving almost the same treatment?

(pause, listening)

Uh huh, or that the forms used to say that, but, oh, we just went and took it out along the way? And, oh, by the way, we forgot to tell anyone?

(pause, listening)

Sure, Eli was absolutely convinced he was doing the right thing – but he also didn't expect to die! He didn't know he was ineligible!

(pause, listening)

That's what I say, they had to know there's only so far you can push the dosage up before somebody's going to die. But even before that, to give deceptive consent forms to an 18-year-old, it's beyond words....

(pause, listening)

You're not the only one wh's said that to me. Now everybody's talking about a financial conflict of interest. They had the patents and the little biotech company, all ready to go.

(pause, listening)

It was all about money. Everyone's telling me to sue. I don't know yet – but whatever happens, it's payback time.

ELI

Hugh – can ya hear me? Radio to Hugh... are you receiving... No, I didn't think you'd tune in to Radio Free Eli, broadcasting 24-7 on your FM dial... but I'll tell you what, I have no problem picking up signals – I think I'm on the God-channel. In fact, I have some guy reading me poems all the time. I didn't even like poetry. I didn't even like English class! Anyway, Hugh, this one's for you:

THE VOICE

The long drift has ended in tumult,
imparting you in the deluge,
the swell that's overcoming you,
filling your nostrils,
it's just the rise and fall.
You will breathe moist sweet air again,
your broadcast upon the waves
running through the irresistible blue.

Scene 5. US Senate

*Senator, FDA official Hugh, patients' advocate Eli,
Hearing discusses the recent FDA judgements and what needs to change*

DR. VAN DESAI (p)

(addressing the senators)

Mr. Chairman, it is my strong belief that if violations have occurred, the responsible parties should face the consequences. To restore the public's confidence in clinical research and in a federal regulatory agency like the FDA, charged with patient safety, it is essential that any violation of approved procedures be dealt with swiftly and appropriately.

Gene therapy offers an unprecedented modality of medicine with enormous potential. It is a young science which is just beginning to show the fruits of its labor. We still have a long way to go. We must learn from our mistakes, but continue to move forward to harvest the untapped potential of this novel technology to reduce the burden of human disease.

HUGH (p)

(addressing the senators)

Dear Senators:

I am addressing this committee in the hope of bringing to light some very serious concerns that I have as a result of my son's death....

He believed after discussions with the representatives from Franklin that the worst that could happen in the trial would be he would have flu-like symptoms for a week. He was also told that the most dangerous parts of the procedure were the catheterization procedure by which the genetic material would be introduced to his liver, and the liver biopsy that was to be done a week later. With the knowledge I had at that time I was comfortable enough to send my son

(continued on next page)

Eli was excited to help. He relied on my judgment in participating in this clinical trial and I trusted this to be a well controlled and purely ethical effort. Less than 24 hours after they injected Eli with the vector in an amount only one other person had ever been given, Eli's entire body began reacting adversely. He went into a coma before I could get to Philadelphia and see him and died two days after my arrival directly as a result of that gene therapy experiment.

While his death has been a devastating blow to us, his example has sustained us through it all.

As you can imagine, my family and I have many concerns over what happened to Eli. Eli and I were told in late July 1999 that a prior patient had shown a clinical improvement of 50 percent in her ability to eliminate ammonia from her system following gene therapy. At the Recombinant DNA Advisory Committee meeting in December, I discovered that no efficacy was achieved at all in this patient. We were also unaware of the severity of liver injury incurred by several of the patients prior to Eli.

I learned, after Eli's death, that Franklin had removed from the information they gave Eli and me any reference to deaths of monkeys, which had previously appeared in their documents. At the RAC meeting in December I learned that at least one other monkey died in a related study using the same adenoviral vector used on Eli.

I learned that Franklin neglected to follow its own and FDA protocols when it found that Eli had ammonia levels above the permissible limits, a clear danger sign, and yet went forward with the procedure anyway.

I had very close contact with the doctors involved until December 10, 1999 just after the RAC meeting. Looking back, I can see that I was very naïve to have been as trusting as I was.

I have read that my son's death has been called by one of the leaders in this field as “a pothole” on the road to gene therapy. His death was no pothole. It was an avoidable tragedy from which I will never fully recover. My concern now is that Eli's death not be in vain, not be just a pothole. I am not against gene therapy. I recognize it holds so much promise for so many people. But we cannot allow what happened to Eli to happen again.

I am not a politically sophisticated man, but neither am I unintelligent when it comes to what motivates people. I understand how important competition is in the world of business, I can understand the temptation to influence government, and I realize the desire of some to make a name for themselves. However, when lives are at stake, and my son's life was at stake, money and fame should take a back seat. The concern should be not on getting to the finish line first, but on making sure no unnecessary risks are taken, no lives filled with potential and promise are lost forever, no more fathers lose their sons.

PATIENTS' ADVOCATE 1

(addressing the senators)

I am also the parent of a child with OTC deficiency. You must to allow the research to continue. It is our only hope. My son said to me as I left my house this morning, "Mom, please tell them I want the have gene therapy. I hate being sick."

PATIENTS' ADVOCATE 2

(addressing the senators)

Senators, all my life I have suffered from cystic fibrosis. I'm still here. But I'm worried. I'm worried that if the science is slowed down too much, a cure will come too late for me. My battle with CF is a race. Don't let me lose that race when the finish line might be just around the corner.

Scene 6. Franklin University

DR ROBERT VIRDEN

(making a public statement)

There were what we believed to be largely minor breaches of filing forms at particular times, but those in no way contributed to this unfortunate and tragic event. Based on our retrospective, careful in-house review, we have not found any evidence at all that things would have been changed if these minor deviations had not occurred.

It wasn't that they weren't carefully following what they were doing. It was just that, in truth, in regard to those issues, they could have done better.

We understand that nothing less than the highest possible standards for the conduct of research are acceptable at Franklin University. The thoughtful process that has led to our response to the FDA is an important step which, together with the other important initiatives underway, will ensure that the conduct of research at Franklin does, in fact, meet those standards.

Scene 7. Heaven

ELI

This isn't so bad now. They're telling me I'm a saint. "Mr. Eli Schroeder is a hero who gave his life for a cause in which he believed deeply." How do you like this one? Senator Kennedy: "He had the courage to put himself at risk to test what he deeply believed to be the best hope of a cure for those with genetic disorders." Well, I can't say it was exactly like that, but I'll take it on my tombstone anyway.

But me, I keep asking myself, am I mad at the things they did wrong? Well, the rules of the game have changed for me, or else I'd say yes. But none of those things take away from the good stuff that my life brought – it wasn't me doing it, I was just playing a role. Anyway, down on the playing field, no more denials now – the jury's in.

Scene 8. Franklin University

MOORE

(making a public statement)

Our clinical research programs at Franklin University must meet the highest possible standards for academic excellence and patient safety and care. Nothing less is acceptable. We are extremely grateful to the members of our investigating committee, who brought their collective insight and considerable experience to the task.

CHGT is a site of important research on a therapy that may provide great benefits to human beings in the future, and we will continue to support it. The University has greatly benefited from the committee's questions about the scope of the CHGT, and its role in the conduct of research using human subjects at the University.

Franklin and the CHGT have jointly determined that CHGT can best serve the important future of gene therapy by resolutely focusing on molecular and cellular work and animal model experimentation. (With emphasis:) CHGT will not conduct human clinical trials in the future.

Scene 9. President Clinton announces new safeguards

PRESIDENT CLINTON

(from tape)

Today I am instructing the FDA to take new actions designed to ensure that individuals are adequately informed about the potential risks and benefits of participating in research, and steps designed to address the potential financial conflicts of interest faced by researchers. We are also sending the Congress a new legislative proposal to authorize civil monetary penalties for researchers and institutions found to be in violation of regulations governing human clinical trials. If this legislation passes, FDA will, for the first time for drugs and biologics, have the power to fine researchers and their institutions, up to \$250,000 and \$1 million respectively.

Scene 10 Philadelphia Courthouse

HUGH

(making a public statement)

I want to express my satisfaction with the outcome of today's legal settlement with Franklin University; but also my sadness. I have undergone a painful change of heart in the year after my son's death. At first, I fully trusted the researchers and held them blameless. But gradually, as disclosures of wrongdoing emerged, I concluded that I had been duped by scientists who cared more about profits than safety.

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Dealing with the money end of this settlement was probably one of the most difficult aspects of this whole thing, because this experiment *was all about money*, and it was never about money for Eli. I do not believe that this settlement will bring any real closure to my family and me. There's never really any satisfaction to be had. But I am encouraged by the changes that have happened in recent months. I am just amazed at the impact that my boy has had.

Scene 11. Center for Human Gene Therapy

FERRIS

(to himself)

It wasn't about money – Hugh's wrong. But I'm sorry. I'm just so sorry. All along I've been saying, "I can't believe this is happening to me," but now I see none of it would have happened if I hadn't made it happen. Eli, I'll always have you hanging over me, reminding me. Eli, if you're out there somewhere, forgive me. I'll try to bring about the cure you wanted so bad.

ELI

Alright, doc. Stick to the molecules. Genes and proteins. Someone else gets to play with the bodies now. But it's better this way. I think you're gonna find a whole other way of doing it. It will take a long time. But we have all the time in the world. You're learning to be patient.

THE VOICE

We flowering particles, we endless grains –
how wide open, how boundless – and –
how transient our doings,
and our scattered remnants:
how each breath of wind in our ears,
each stalk voices its "yea" to us,
affirms our momentary stake
in the unyielding sea of change.

END

CHARACTER KEY

- Dr. Raymond Ferris = Dr. James Wilson, director, Institute for Human Gene Therapy, University of Pennsylvania, Philadelphia
- Eli Schroeder = Jesse Gelsinger, 18-year-old patient who dies in gene therapy trial
- Hugh Schroeder = Paul Gelsinger, Jesse's father
- Dr. Sarah Moore = Dr. Jean Rodin president, University of Pennsylvania
- Dr. Carla Zetta = Dr. Kathryn Zoon, FDA regulator
- Dr. Andrew Ireland = Dr. French Anderson, gene therapy pioneer and booster
- Dr. Van Desai = Dr. Inder Verma, president, American Society of Gene Therapy
- Dr. Robert Virden = Dr. Richard Tannen, Franklin University Medical School Senior Vice Dean