CHEMGENES EXHIBIT 2003 Shanghai Hongene v. ChemGenes Case IPR2023-00875



Transcript of Phil S. Baran, Ph.D.

Date: January 22, 2024 **Case:** Shanghai Hongene Biotech Corporation -v- Chemgenes Corporation (PTAB)

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> > WORLDWIDE COURT REPORTING & LITIGATION TECHNOLOGY

1 UNITED STATES PATENT AND TRADEMARK OFFICE 2 3 BEFORE THE PATENT TRIAL AND APPEAL BOARD 4 5 SHANGHAI HONGENE BIOTECH CORPORATION, 6 Petitioner, 7 v. 8 CHEMGENES CORPORATION, 9 Patent Owner. 10 11 IPR2023-00862 U.S. Patent No. 8,541,569 12 IPR2023-00875 13 14 U.S. Patent No. 8,309,707 15 16 17 VIRTUAL DEPOSITION OF PHIL S. BARAN, PH.D. Monday, January 22, 2024 18 19 8:05 a.m. EST 20 Job No.: 521578 21 22 Pages: 1 - 188 23 Reported by: Monique Vouthouris, CCR, RPR, CRR 24 25

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5	DEPOSITION OF PHIL S. BARAN, PH.D.,
6	pursuant to notice, conducted virtually via Zoom
7	Videoconference, before Monique Vouthouris,
8	Certified Court Reporter, Registered Professional
9	Reporter, Certified Realtime Reporter, and Notary
10	Public in and for the States of New Jersey and New
11	York.
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1	A P P E A R A N C E S
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3	ON BEHALF OF PETITIONER SHANGHAI HONGENE
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3		Vice President and General Counsel
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5		ANUJ MOHAN SRIVASTAVA, ChemGenes COO
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10	Exhibit 2036 Chemistry World article September 103
11	21, 2021, "Phosphorus(v) method
12	to make unnatural
13	oligonucleotides rivals industry
14	standard," by Kira Welter.
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1	PROCEEDINGS
2	
3	THE COURT REPORTER: Good morning. My
4	name is Monique Vouthouris, representing Planet
5	Depos.
6	Today's date is Monday, January 22, 2024.
7	We are here for the deposition of Dr. Phil S. Baran,
8	in the matter before the Patent Trial and Appeal
9	Board, Shanghai Hongene Biotech Corporation,
10	Petitioner v. ChemGenes Corporation, Patent Owner,
11	IPR2023-00862 and IPR2023-00875.
12	Will counsel please identify themselves
13	and state whom they represent.
14	MR. SHORES: This is Dan Shores with
15	Rothwell, Figg in Boston, in our Boston office, and
16	with me here today is Adam Nicolais, who is in our
17	DC office, and we represent
18	MR. EDWARDS: Go ahead, Dan.
19	MR. SHORES: the patent owner, we
20	represent the patent owner.
21	MR. EDWARDS: Dan this is Jeremy
22	Edwards from Procopio, Cory representing the witness
23	and the petitioner.
24	Dan, I think you may also have some party
25	representatives joining us. Could you identify

1	them, please, for the record.
2	MR. SHORES: Yes. Thanks. Thank you,
3	Jeremy. Yes, also joining here via Zoom is Anuj
4	Mohan, who is the COO from ChemGenes, and also
5	joining is Kevin O'Connor, who is the general
6	counsel at ChemGenes, and also Jeremy Little from
7	ChemGenes Corporation.
8	PHIL S. BARAN, PH.D.,
9	being first duly sworn or affirmed by the Notary,
10	testifies as follows:
11	EXAMINATION
12	BY MR. SHORES:
13	Q Good morning, Dr. Baran.
14	A Good morning.
15	Q Or is it good afternoon? I don't know
16	what the time
17	A No, it's 10 o'clock here.
18	Q All right. So we're not that far off
19	sync.
20	A No.
21	MR. SHORES: So today's deposition will be
22	this is a statement for the record.
23	Today's deposition is being taken in
24	connection with two IPR proceedings. And this is
25	something that we, counsel Hongene counsel and I

1	have discussed before, you know, going on the
2	recording, going on the record. But the IPR, this
3	single deposition sitting will be for IPR2023-00862
4	relating to U.S. Patent Number 8,541,569 and IPR
5	number 2023-00875, relating to U.S. Patent Number
6	8,309,707.
7	And while we reserve the right for the
8	full seven hours for allotted to patent owner for
9	each examination, we believe, with everyone's
10	cooperation, that we will not have to use the full
11	allotted time and can conduct the depositions for
12	both matters today here in one sitting.
13	So I wanted to state that for the record.
14	BY MR. SHORES:
15	Q So, okay, Dr. Baran, so we've we've had
16	a previous deposition together, and we went over
17	some ground rules.
18	Do you remember those ground rules that we
19	covered?
20	A Yes, sir. Yes, sir, I do.
21	Q Okay. I'm not seeing a need to really go
22	through all of those, but I will touch on a few of
23	them.
24	You understand you're under oath, correct?
25	A Correct.

1	Q Okay. You understand that this deposition
2	is being videotaped via Zoom, right?
3	A Correct.
4	Q And you understand that counsel can make
5	concise objections to my questions, but your counsel
6	is not allowed to make speaking objections or to
7	coach you on your answers.
8	Do you understand that?
9	A Yes.
10	Q And you understand that unless counsel
11	instructs you not to answer my questions, unless
12	it's for the purposes of privilege, you must answer
13	my questions.
14	Do you understand?
15	A Yes.
16	Q Is there any reason why you feel you would
17	not be able to provide full, truthful testimony
18	today?
19	A No, sir.
20	MR. SHORES: Okay. Okay. I would like to
21	introduce previously marked Petitioner's Exhibit
22	1003, for the '569 for the matter relating to the
23	'569 patent.
24	(Exhibit 1003 ('569 IPR) marked for
25	identification.)

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1 Q And then, Dr. Baran, can you see this 2 Exhibit? 3 MR. EDWARDS: I believe the witness is 4 muted. 5 Yes, I can. Sorry, my mute -- my audio Α 6 button disappeared, so I'll just leave it on. 7 No problem. And then are you able to Ο 8 navigate this document? 9 No, but I can open the same document, if А 10 you would like, and be able to navigate it, whatever 11 you like. 12 Q Okay. I would like you -- maybe the technician can give you control to be able to 13 navigate on your end. 14 15 THE TECHNICIAN: Yes. The witness does 16 have remote control and we can see the cursor moving 17 So you should be able to -- yes. around. 18 Do you want to see how --0 That's cool. I've never done that before. 19 Α Super cool. Okay. Great. 20 Okay. 21 Q 22 Α Awesome. 23 Q And so do you recognize this document, 24 Dr. Baran? 25 Yes, sir. Yes, I do. Α

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1	Q And this is a copy of the declaration you
2	submitted in IPR2023-00862, right?
3	A Correct.
4	Q Okay. If you move down to page 45 of
5	the page 45, which is the legend at the bottom.
6	A Sorry. There's a little lag here.
7	Q Right.
8	A 45, 43. One second.
9	Q 45.
10	A 45. With my signature, okay.
11	Q Right. And that statement says, "I
12	declare under penalty of perjury under the laws of
13	the United States of America that the foregoing is
14	true and correct."
15	And is that your signature?
16	A Yes, sir.
17	Q Okay. And so is it correct that you
18	reviewed and verified the statements in this
19	declaration before you signed this declaration?
20	A Yes. There is, though let me see if
21	this is the one that has some typos. No, this one
22	is good. Yeah, the other one has some typos in the
23	table of contents.
24	Q Yes.
25	(Court Reporter clarification.)

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1	THE WITNESS: I hear you loud and clear.
2	Q Okay. So for this Exhibit 1003 for the
3	'569 patent, you still agree with the statements
4	that you made in your declaration; is that correct?
5	A Yes, sir.
6	MR. SHORES: Okay. So if we can now take
7	this exhibit down and put up Exhibit 1003 from the
8	IPR involving the '707 patent.
9	(Exhibit 1003 ('707 IPR) marked for
10	identification.)
11	Q Dr. Baran, do you see this?
12	A Yes, sir, I do.
13	Q And is this a do you recognize that
14	this is a copy of the declaration that you submitted
15	in IPR2023-00875?
16	A Yes, this is it.
17	Q Okay. And then if you go to page 48.
18	A Okay.
19	Q Do you see where it says, "I declare under
20	the penalty of perjury under the laws of the United
21	States of America that the foregoing is true and
22	correct"?
23	Do you see that?
24	A Yes, I do.
25	Q I read it correctly?

	, , ,, , ,, , ,, , , , , , , , , , , , , , , , , , , ,
1	A Yes.
2	Q And that is your signature?
3	A Yes.
4	Q Okay. And I believe you said earlier that
5	you had some comments on some typos that you wanted
6	to point out?
7	A Yeah. The I didn't do this table of
8	contents. It was a clerical error on the Procopio
9	side. But as you can see here, all of these error
10	things are like from Word. This table of contents
11	is a little messed up. But I didn't the contents
12	of the document is correct. It's just the table of
13	contents is a little screwy. Sorry about that.
14	Q Microsoft Word has its own skill set some
15	aspects, so
16	A Indeed.
17	Q Okay. So other than the errors in the
18	table of contents and other I guess typographical
19	errors, you still agree with the statements that you
20	made in this declaration; is that correct?
21	A Yes, sir.
22	Q Okay. Thank you.
23	Okay. Now, you've you have, you know,
24	published papers, and, you know, a number of pages,
25	over 250 papers you've published. And you've

1	you've published also in regard to oligonucleotides,
2	you've published papers relating to $P(V)$ $P(V)$
3	chemistry; is that right?
4	A We've published on P(V), and as part of
5	that, done P(III) chemistry as well. In general,
6	oligonucleotide synthesis at large.
7	Q Okay. But with respect to P(V), you've
8	published on P(V) before, right?
9	A In those publications there's P(III)
10	chemistry in there as well.
11	Q Understood. Understood. But I just want
12	to talk about P(V) right now.
13	Would you consider P(V) to be an area that
14	you've, you know, an area of expertise of yours,
15	P(V) chemistry as it relates to reagents used in
16	oligonucleotide synthesis?
17	A I wouldn't put myself in a sandbox on P(V)
18	only. I've consulted broadly on P(III) for well
19	over a decade, that's how I was aware of problematic
20	aspects of certain parts of P(III).
21	So I would consider myself well-versed on
22	P(III) chemistry, P(V) chemistry, the history of
23	oligonucleotide synthesis, which actually originated
24	with P(V), not P(III). So, yeah, I think regardless
25	of the phosphorus oxidation state, I'm well aware of

1	
1	the field.
2	Q With respect to P(V), I mean, do you
3	consider yourself to be an expert in P(V) chemistry
4	as it relates to a reagent for use in
5	oligonucleotide synthesis?
6	A Yeah. As I said P(III), P(V), either one,
7	mm-hmm.
8	Q So the answer is is it yes, that you
9	are an expert in P(V) chemistry as it's utilized as
10	a reagent for oligonucleotide synthesis?
11	A Yeah.
12	Q Okay. And you and your some of your
13	colleagues won the Edison Patent Award last year,
14	right?
15	A Yes.
16	Q Congratulations.
17	A Thanks.
18	MR. SHORES: And so if we can pull up
19	Exhibit 2034 for Dr. Baran.
20	(Exhibit 2034 marked for identification.)
21	Q And this is do you see this document
22	A Yes.
23	Q Dr. Baran?
24	A Yes, I do.
25	Q And have you seen this document before

1	today?
2	A I don't I don't recall reading this
3	document, no. I don't
4	Q Why don't you take a few minutes sorry
5	to interrupt. Do you want to take a few minutes to
6	scan it, that's fine.
7	A It's okay. You can go to your question.
8	Q Okay. Sure. On this page here, which
9	we
10	A Sorry.
11	Q That's okay.
12	I guess that would be page 3 of the PDF,
13	which is with the heading "2023 Edison Patent Award
14	Winners." Do you see where it says "Bristol-Myers
15	Squibb"?
16	A Yes.
17	Q Would you mind I'm sorry. Do you see
18	where it says "Bristol-Myers Squibb" and it says
19	actually, could you read that into the record, that
20	first sentence?
21	A Sure. It says, "Bristol-Myers Squibb and
22	its inventors, Michael Schmidt, Martin Eastgate, Bin
23	Zheng, Ivar McDonald, former employees Richard Olson
24	and William Ewing, along with Scripps Research
25	inventors Phil Baran and former Scripps Research

1	inventors Kyle Knouse and Justine de Gruyter, were
2	recognized with a patent award in the biotechnology
3	category for 'Phosphorus (V)-based reagents,
4	processes for the preparation thereof, and their use
5	in making stereo-defined organophosphorous (V)
6	compound.'" And then U.S. 11,613,554.
7	Q Okay. Thank you.
8	And are you proud of this award?
9	A I'm not really proud of any awards, but
10	that's just a personal thing. I have no role in
11	nomination for this. In fact, I actively discourage
12	anyone from nominating me for anything.
13	MR. SHORES: Okay. If we can pull up
14	Exhibit 2035, please.
15	This looks like it's labeled Exhibit 2034,
16	but this is actually the Exhibit 2035 I was seeking
17	to discuss.
18	THE WITNESS: Okay.
19	MR. SHORES: So just for the for our
20	technician.
21	(Exhibit 2035 marked for identification.)
22	Q So, Dr. Baran, do you see this patent?
23	A Yes, sir.
24	Q And is this the same patent that was
25	referenced in the article we just looked at?

1	A Yes, sir.
2	Q Okay. And the title is "Phosphorus
3	(V)-Based Reagents, Processes for the Preparation
4	Thereof, and Their Use in Making Stereo-Defined
5	Organophosphorus (V) Compounds," right?
6	A Yes.
7	Q I read that correctly, right?
8	A Yes, sir.
9	Q And so this patent what is this patent,
10	you know, directed to?
11	A Well, we can go to the claims, but broadly
12	speaking, it's to encompass a new set of reagents
13	that enables the synthesis of not limited to, but
14	mainly focusing on stereo-defined oligonucleotides,
15	but also oligonucleotides that don't have a sulphur
16	atom in them as well. So an alternative method for
17	making phosphorus (V) containing compounds that is
18	advantageous, especially when one cares about stereo
19	purity at the internucleotide bond when you've
20	got a phosphorothioate, for example.
21	(Court Reporter clarification.)
22	A When you have got a phosphorothioate
23	specifically.
24	Q Okay. And if we can turn to it would
25	be the fourth page of the PDF here.

Transcript of Phil S. Baran, Ph.D. Conducted on January 22, 2024 Okay. I'll try to scroll down. 1 А 2 Q So it would be Figure 2. 3 Here we go, how's that. Α 4 That's good. And actually, just the next Q 5 one. 6 The next one, okay. А 7 0 Yeah, Figure 2. Okay. 8 So what does this figure represent, 9 Dr. Baran? 10 Α This figure represents a general cycle for 11 the use of P(V)-based scaffold to form in a 12 canonical coupling cycle form oligonucleotide bond 13 linkages wherein there is stereo control at the 14 phosphorus atom. 15 0 Okay. So if we look at the top, I guess 16 looks like there's a compound above that's listed above load? 17 18 А Yes. 19 Q And what is that compound? That would be a nucleoside with a free 5 20 А 21 prime OH group and it is connected at the C3 prime 22 to a resin solid. 23 Q So like a solid support? Exactly, mm-hmm. 24 Α 25 And so then that's like a starting Q

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1	compound?
2	A Yes, sir.
3	Q And is that something that is I mean,
4	is that a complex compound or that's something
5	that's just easily synthesized or can get off the
6	shelf? Like, how would you describe that that
7	compound?
8	A Well, it depends on the nature of the
9	linker and the resin. In general, it's a standard,
10	you know, standard type of compound that one would
11	prepare. Certainly not one that would be, you know,
12	of difficulty or complexity for a POSA to prepare.
13	Q It's not a phosphoramidite, though, right?
14	A No.
15	Q So it's just it has a nucleoside solid
16	support, which is the resin, and then at the I
17	guess at the I guess that's the 5 prime it will
18	have the OH?
19	A Correct.
20	Q Okay. And then the compound to the right
21	of that, I guess, I guess at 1 o'clock or 2 o'clock,
22	or the next compound as you go in the clockwise
23	direction, what is that compound?
24	A That is what we would refer to and I'll
25	say it slowly as an oxathiaphospholane ring

1	system.
2	Q Okay. And is that compound, which I am
3	not going to attempt to restate what you just said,
4	but is that compound, you know, a compound that
5	you you helped develop?
6	A Compounds of this sort are what are part
7	of the key part of the invention. One of them is
8	depicted here, but there are many others in the
9	that are claimed of this ring type.
10	Q Okay. And then so what happens in the
11	next step, you know, as you continue to go clockwise
12	in this Figure 2 of the '554 patent?
13	A Certainly. So the next step is the
14	loading of that oxathiaphospholane ring system on to
15	that 5 prime OH.
16	Shall I continue?
17	Q Yes, please.
18	A And then continuing on, another nucleoside
19	is coupled generally, again, at the 3 prime 30H, and
20	that leads to a coupling event that then liberates
21	the oxathiaphospholane ring system by what we depict
22	here as a self-immolation, which basically means it
23	falls apart and liberates the in the case of X
24	equal to O and Y equal to S, a phosphorothioate
25	internucleotide bond.

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1	Following that, the DMT, or trityl,
2	usually a DMT, is de-protected under acidic
3	conditions, and that then liberates another 5 prime,
4	which can be brought into the same cycle again.
5	Q And then this continues to cycle and then
6	you build oligonucleotide this way, right?
7	A Exactly.
8	
9	backbone, which I believe is depicted under C5 prime
10	deprotection, that compound that's below C5 prime
11	deprotection, do you see that?
12	A Mm-hmm. Yes.
13	Q And is there there's a backbone
14	depicted there, oligonucleotide backbone?
15	A Well, once you get to what's depicted
16	here is a dinucleotide.
17	Q Okay.
18	A And an oligo would be two or more. So as
19	you continue to cycle, you stop whenever you reach
20	your desired length. But anything two or more is
21	considered an oligonucleotide. Although if you're
22	only making two, I would call it a dinucleotide.
23	Q Okay. So understood.
24	So this is a vertebrae, I guess, if we're
25	talking bones and

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1	A Yeah.
2	Q And that vertebrae or component or the
3	linker for that one monomer is depicted there.
4	Is that a natural backbone or vertebrae
5	of, in other words, what you would find in native
6	RNA or DNA, the P equals X PY?
7	A Well, it if X is equal to O and Y is
8	equal to O, that is a naturally occurring
9	phosphodiester, the type that underlies all the DNA
10	in our bodies or in nature.
11	Now, if X is equal to O and Y is equal to
12	S, or vice versa, however you want to draw the
13	resonance, that is a phosphorothioate. And to my
14	knowledge, those don't exist in nature. Those were
15	invented 30, 40 years ago by a gentleman by the name
16	of Stec, I believe he was the one who invented it.
17	S-t-e-c.
18	And the purpose of the phosphorothioate
19	and stop me at any time if I'm going too deep the
20	purpose of
21	Q No.
22	A Okay. The purpose of the phosphorothioate
23	is to prevent these oligonucleotides from being
24	degraded very quickly by nucleases. So the main
25	breakthrough that was made many years ago, that

1	enabled compounds like this to be given to patients,
2	was the introduction of the stable internucleotide
3	bonds that don't get rapidly degraded, and, thereby,
4	allowing for an actual clinical use of these things.
5	Q Right. So there is a is it fair to say
6	there was a the modification to, and we'll refer
7	to it as the backbone because, you know, just assume
8	that it's oligonucleotide, but the modification to
9	the backbone is something that would help with
10	respect to therapeutics; in other words, the it
11	will be let me back up a second. Let me forget
12	that question.
13	Is it fair to say that these the
14	modified backbone, as it's depicted here, and if
15	it's not naturally occurring, the modified backbone
16	would be useful in therapeutics?
17	A It could be useful in therapeutics most
18	significantly, but it could also be useful for
19	diagnostics or probes or for an academic publication
20	where one is trying to, you know, probe some sort of
21	in vitro analysis.
22	So it could have a variety of uses. The
23	most famous of them would be this enables you to use
24	such compounds in a human or veterinary or medical
25	scenario.

1	Q So is it fair to say that the difference
2	between a natural oligonucleotide that, you know,
3	say, for example to to RNA, that has native
4	phosphodiesters, that would react a lot differently
5	than a modified oligonucleotide, you know, to say
6	RNA, that uses phosphorothioates?
7	A React differently in the context of the
8	body as a therapeutic, yeah. So
9	Q And you might have explained sorry to
10	interrupt.
11	A No, no. That's all right. I mean, it
12	just incurs a much higher level of stability so that
13	your body doesn't instantly just chew it up with
14	nucleases like Pac-Man and then it's gone.
15	Q Okay. Okay. I get it.
16	So it's a modification that was made
17	modification that was made to to have higher
18	stability, you know, as compared to the natural
19	phosphodiester
20	A You got it, yes.
21	Q Okay. And so this process coming back
22	to Figure 2, this process can be applied and can
23	produce an oligonucleotide with native
24	phosphodiesters, right?
25	A Exactly.

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1	Q And also it can produce oligonucleotides
2	with phosphorothioates as well.
3	A Exactly, you got it.
4	Q And would you say that a key to the
5	invention is and you might have said this
6	already but a key to the invention is the fact
7	that it can be used to create oligonucleotides with
8	having the phosphorothioates?
9	A That's not the key, because you can use
10	P(III) people use P(III) all the time to make
11	phosphorothioates. However, it's very difficult to
12	control the stereochemistry when you do so.
13	So the key part of the invention is really
14	a few-fold. Number one, it can enable you to get
15	when you desire a phosphorothioate, high, complete
16	stereo purity at that internucleotide bond.
17	Number two, the rate of the couplings are
18	competitive with or on par with the super fast
19	kinetics of P(III) chemistry.
20	And number 3, the preparation of these
21	compounds is very simple and the intermediates are
22	stable and crystalline. And because you're going
23	through P(V), there are some efficiency advantages
24	that you can that are apparent relative to
25	P(III).

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1	Q And what are the what would you say the
2	key differences between this approach and the P(III)
3	approach, phosphoramidite approach?
4	A Well, first, on first principles, you're
5	no longer dealing with an oxidation state change.
6	So in the canonical coupling cycle for P(III),
7	there's going to be an oxidation step where you need
8	to take P(III) to P(V), number one.
9	Number two, often there's extra protecting
10	group chemistry needed for P(III), which you don't
11	have in this invention.
12	And number three, it's often very
13	difficult to get complete stereo purity when you're
14	using P(III); whereas, the P(V) manifold outlined in
15	this patent and the related publications is
16	demonstrated to give to the limits of analytical
17	detection only one isomer at phosphorus.
18	Q And isn't it correct that P(V) chemistry
19	is sort of like isn't that isn't that how
20	isn't P(V) chemistry occurring naturally?
21	A Sure. In fact, there are very few
22	examples in nature of P(III) oxidation state. There
23	are P(III) exists in nature. There's some rare
24	examples of it in biosynthesis. You know, on the
25	planet Venus I think the atmosphere has a lot of

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1	P(III) in it. But in general, the building blocks
2	of nature that keep us all alive here today are
3	based on P(V) chemistry.
4	Q Based on P(V). But is your is this
5	chemistry, this breakthrough, does it mirror nature?
6	How is it different than nature?
7	A Oh, well, first, nature doesn't make
8	phosphorothioates, to my knowledge. I don't know, I
9	mean, maybe there's some random publication out
10	there that shows that there's a phosphorothioate in
11	nature. I don't know. I haven't seen it
12	(Simultaneous speaking.)
13	A Yeah.
14	Q I'm sorry. You go ahead. You finish your
15	answer.
16	A But nature generally doesn't make
17	phosphorothioates. You certainly don't find any in
18	a biological organism like a dog or a cat or a human
19	where the body is making phosphorothioates. So that
20	is the first fundamental difference.
21	But if we're just talking about a
22	phosphodiester, then, sure. Nature uses you
23	know, her way of making oligonucleotides is solely
24	through the use of P(V), mm-hmm.
25	Q And is it correct that the first DNA

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1	sequences were synthesized using P(V), the P(V)
2	approach?
3	A Yeah. And I think I outline that history
4	in my declaration, mm-hmm.
5	Q And tell me about how, you know, how and
6	why the field moved to P(III).
7	A Well, the breakthrough in the '70s by
8	people like Letsinger and Caruthers and Beaucage,
9	many others, there were many involved, Caruthers is
10	the paramount figure in that area, was the finding
11	that the coupling rates were far faster with the
12	phosphoramidite P(III) reagents, and that led to a
13	revolution. And companies like, you know, Hongene
14	and ChemGenes and Glen and all the other, you know,
15	famous oligo reagent suppliers, and as well as a lot
16	of companies that make oligonucleotide machines,
17	were born as a consequence of the, you know, awesome
18	power and great coupling efficiency of P(III)
19	chemistry. So it definitely was a revolution in the
20	field.
21	Q And how do you view P(V) chemistry
22	vis-a-vis P(III)? Is this the next generation?
23	How would you describe the P(III)
24	platform P(V) platform? Excuse me.
25	A When you say the P(V) platform, are you

1	referring to what we've patented?
2	Q Yeah, sure, we can use that as an example,
3	what's been patented. Like, for example, this, you
4	know, reagents relating to the compound that's shown
5	in Figure 2.
6	A Well, these are newcomers to the block.
7	What I can say is that a lot of companies
8	are using it for the purpose of generating
9	stereopure internucleotide bond linkages. I think
10	it's complementary to P(III). It has some distinct
11	advantages which is why many companies have started
12	to use it.
13	But as I said, it's complementary. So I
14	don't think we're going to see this disappearance of
15	P(III) chemistry any time soon. But it's just
16	you know, organic chemists like to engage in the
17	practice of giving the practitioner, in an academic
18	setting like we did, of giving the practitioner
19	other options.
20	So never in our studies was the goal, oh,
21	we're going to do something that will make P(III)
22	obsolete. Rather, it's just, oh, here's something
23	that could be really useful, that's it.
24	Q And it would give chemists an option; they
25	could use either the P(III) phosphoramidite or they

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1 could use the P(V) reagent? 2 Α Precisely. 3 Okay. But you're not proud of this --Ο 4 you're not proud of this achievement? 5 Α I'm proud of my students. I'm proud of, 6 you know, when the lab is able to do something 7 useful. But, I mean, it's -- this is not -- this is 8 a deposition on facts, not on psychology. But my 9 psychology is just I, you know, I don't rest on 10 laurels and pride comes before a big fall. So I do 11 work, I hope it's useful, and then I move on. 12 Q Okay. MR. SHORES: All right. Could we see 13 Exhibit 2043. Okay. 14 15 (Exhibit 2043 marked for identification.) 16 Dr. Baran, this is another exhibit marked 0 17 Exhibit 2043. 18 Do you recognize this document? Yes, sir. 19 А 20 Ο And what is this? 21 Α This is another chapter on P(III) 22 chemistry. In this case, related reagents are used 23 now to make carbon phosphorus bonds, again, with 24 high stereo purity by taking advantage of the P(V) 25 oxidation state.

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1	Q Okay. And this is a patent application,
2	to your understanding, right?
3	In other words, have you been notified
4	I'm sorry. Do you recognize this as being a patent
5	application?
6	A Patent application, yes. I don't know if
7	the patent was granted or not. I don't I have no
8	idea.
9	Q Okay. Is this relating to the same work,
10	this patent application, does it relate to the same
11	work that was conducted in connection with the '554
12	patent?
13	A It's related. It's a very it's a
14	different spin on things. So the prior work we just
15	talked about was focused on internucleotide bond
16	linkages, making oligonucleotides, forging
17	phosphorothioates
18	(Court Reporter clarification.)
19	A So the prior work was focused on making
20	oligonucleotides, phosphodiesters,
21	phosphorothioates, those kinds of those kinds of
22	heteroatom phosphorus bonds. In this work, we were
23	focused on making carbon phosphorus bonds in a
24	stereo-defined fashion.
25	Q Okay. And to your knowledge, there hasn't

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1	been a patent granted relating to this application;
2	is that right?
3	A I don't know. I don't follow it.
4	Q Okay. Did you participate in the in
5	the drafting of this? Did you review any of the
6	drafts, for example?
7	A Yes. We deposited, you know, the we
8	gave to the attorney I forget if the attorney was
9	at Scripps or was at BMS. I think it was at BMS,
10	Elliot was his name, I think. We, you know, gave
11	all of our data and the publication before it came
12	out, all that text. And then the attorney turned
13	that into a patent draft and we all reviewed it,
14	that kind of thing.
15	Q And did you go through that same or
16	similar process with respect to the '554 patent?
17	A Yes, sir.
18	Q And do you recall signing an oath or
19	declaration in connection with the '554 patent?
20	A Yes, we signed for everything. Yes.
21	Q You recall signing an oath or declaration
22	in connection with this application here, the
23	Exhibit 2043, which is application 17/758898?
24	A Yes, sir.
25	MR. SHORES: If we can pull up Exhibit

1	2044.
2	(Exhibit 2044 marked for identification.)
3	Q Are you familiar with this document,
4	Dr. Baran?
5	A I believe this is one of the documents
6	this is in the prosecution history of the '885
7	patent?
8	Q Okay. I'll maybe refresh your
9	recollection. This is the patent owner's response
10	that was submitted in connection with the sister
11	proceeding related to the '885 patent. If you want
12	to scroll
13	A Yeah, let me
14	Q I'm going to use a figure in here to aid
15	the aid the examination.
16	A Yeah, yeah, uh-huh. Okay. I do recognize
17	this document. Yes. Okay.
18	Q Okay. And if you could go to page 13.
19	A Okay.
20	Q Okay. And you see there's a what is
21	depicted in the figure on page 13?
22	A It's an oligonucleotide. In this case,
23	RNA, a piece of RNA.
24	Q Okay. Exemplary oligonucleotide; is that
25	fair?

1 Α Yeah. For RNA, yes. 2 Q RNA, okay. And then is -- what type of backbone are we looking at here, what types of 3 4 linkages? 5 Α Those are all phosphodiesters. 6 Okay, phosphodiesters. And we talked Q 7 earlier about those being natural --8 naturally-occurring backbone? 9 А Yes, sir. 10 Ο Okay. And then if we go to page 14, what 11 would you say is depicted there? 12 А You know, you could call it a chimeric oligonucleotide. You could call it an 13 oligonucleotide with, you know, natural and 14 15 unnatural riboses. But it would be correct to call 16 it a chimeric oligonucleotide because it has within 17 it some DNA, some RNA, and some analogs of DNA and 18 RNA. 19 Q Okay. And so if we go to back to page 13, 20 could this oligonucleotide be synthesized using P(V) 21 reagent method that you've invented? 22 Yeah, we have. Other people have as well, Α 23 yes. 24 When you say "other people have as well," Q 25 what do you mean?

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	. ,
1	A Other companies.
2	Q What other companies?
3	A Well, other companies that are making, you
4	know, oligonucleotide analogs are, but I don't know
5	if I can reveal names without breaching
6	confidentiality. I can say, without getting in
7	trouble, my own company, Elsie, has made such
8	compounds using P(V).
9	Q Right. And so, similarly, if you go to
10	page 14, could this oligonucleotide chimeric
11	oligonucleotide be synthesized using P(V) chemistry?
12	A Yeah.
13	Q Okay. This could also be synthesized
14	using phosphoramidites, right?
15	A For sure.
16	Q And then back on page 13, this
17	oligonucleotide could be synthesized using
18	phosphoramidite chemistry, right?
19	A For sure.
20	MR. SHORES: Okay. If we can go to
21	Exhibit 1001 in the '569 IPR. Shifting gears here.
22	(Exhibit 1001 ('569 IPR) marked for
23	identification.)
24	Q And if we can go down to so do you
25	recognize this document, Dr. Baran?

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1	A Yes, sir.
2	Q And what is this document?
3	A This is what I refer to as the '569
4	patent.
5	Q Okay. And if you can scroll down to the
6	claims, which appear at the end
7	A Give me a second to navigate this.
8	Q Yeah. It's pretty fast.
9	Okay. And you see claim 1?
10	A Yes, sir.
11	Q Okay. Could could P(V) reagents be
12	used to synthesize any of the molecules I'm
13	sorry, let me back up.
14	Can we go to column 98, actually.
15	A 98, give me a second. 98, okay.
16	Q Yeah.
17	A Almost there. Okay. 98. Column 98.
18	What line?
19	Q Yeah
20	A I was at 98 and then there we go.
21	Q Yeah, I have to catch up here.
22	A Sorry. There we go. 98.
23	Q And do you see the table that says,
24	"Oligonucleotide sequence synthesized by reverse
25	synthesis method"?

1	A Mm-hmm.
2	Q Could P(V) reagents be used to create this
3	the oligonucleotides set forth in this table?
4	A Well, I need to study. It's possible that
5	we would need to change some of the protecting
6	groups to make the efficiency better. But if you
7	mean could it make the oligonucleotide after it's
8	been completely deprotected, then I think my answer
9	would be yes.
10	But if you want the exact compound that's
11	depicted before deprotection, the yield might be
12	lower because we would recommend using a different
13	protecting group at the 2 prime position.
14	Q Right. And this would be after
15	deprotection, so this is really just
16	oligonucleotide.
17	A Oh, okay. Then my opinion would be yes.
18	Q Right.
19	MR. SHORES: And if we can go to Exhibit
20	1001 of the '707 IPR.
21	(Exhibit 1001 ('707 IPR) marked for
22	identification.)
23	MR. EDWARDS: Dan, you might want to check
24	the sticker, it says "'709" instead of
25	MR. SHORES: Yeah, the exhibit number

1	should be in the parentheses should be '707 and
2	not '709. So we just want to fix that.
3	Q And, Dr. Baran, do you recognize this
4	document?
5	A Yes, sir.
6	Q And what is this document?
7	A This is what we've colloquially referred
8	to as the '707 patent.
9	Q Okay. Thank you. And if you can scroll
10	to column 27.
11	A One second. Getting there.
12	And you said 27?
13	Q Yes, sir.
14	A 27. There we go.
15	Q And you see Table 5 up in the upper left
16	corner?
17	A Yes.
18	Q Could P(V) reagents be used to create any
19	of the oligonucleotides disclosed in Table 5? We're
20	talking about the finished oligonucleotide.
21	A Well, my opinion would be yes.
22	Q Okay. Your understanding is that is it
23	correct that your understanding is that the '707
24	patent and the '569 patent relate to reverse RNA
25	synthesis?

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1	Q And have you ever done that before?
2	A I believe we did do a reverse coupling in
3	the context of making cyclic dinucleotides where we
4	appended where we did do that, yeah.
5	Q When was that? When did you do that?
6	A I think it was in the 2018 science paper,
7	I believe it was in there.
8	Q And when you said "we did that," which
9	group did that?
10	Was that with Scripps?
11	A Scripps and BMS collaborative team.
12	MR. SHORES: Okay. All right. We have
13	been going for about an hour. I finished a line of
14	questioning. Is it okay to take a break now?
15	THE WITNESS: You're the boss.
16	MR. SHORES: Ten minutes? Ten minutes.
17	Okay.
18	(Recess 9:04 a.m 9:12 a.m.)
19	MR. SHORES: If we could put up Exhibit
20	2030, please.
21	(Exhibit 2030 marked for identification.)
22	BY MR. SHORES:
23	Q Okay. Dr. Baran, do you see this Exhibit
24	2030 put up on the screen here?
25	A Yes, sir.

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1	Q And you recognize this document?
2	A Yes.
3	Q Okay. What is this document?
4	A This is one of our publications from 2018.
5	Q Okay. And if you see the you're listed
6	as an author here; is that right?
7	A Correct. Mm-hmm, yes.
8	Q And to the right of your name there's a
9	cross symbol.
10	Do you see that?
11	A Yes.
12	Q And then at the bottom of the paper, the
13	cross symbol indicates corresponding author?
14	A Mm-hmm, yes.
15	Q You're listed there; is that right?
16	A Yes.
17	Q Okay. So what is your understanding, or,
18	you know, what is meant by "corresponding author"?
19	A I mean, the senior corresponding author,
20	the last author is generally the one who is
21	responsible for the vision, the putting the team
22	together, you know, in charge of making sure the
23	data is rigorous and the conclusions are sound, and
24	in this case, you know, wrote wrote the majority
25	of the paper. So basically the person who led the

1	team.
2	Q Okay. And so you were also responsible
3	for reviewing and signing off on this paper; is that
4	right?
5	A Correct.
6	Q Is there anything in this paper that you
7	don't agree with?
8	A I don't think so.
9	Q And if we look at the listing of the
10	authors here, some of these individuals are
11	affiliated with Scripps; is that right?
12	A Correct.
13	Q And which individuals are affiliated with
14	Scripps?
15	A That would be Kyle Knouse, Justine
16	deGruyter, Julian Vantourout, Cian Kingston, and
17	that's it. And they were affiliated with Scripps at
18	the time of the publication, but are no longer in my
19	group.
20	Q Where are they now?
21	A So Kyle Knouse is working at a company
22	that we co-founded together called Elsie. Justine
23	is a lecturer at Texas A&M University. Julian
24	Vantourout is now he was a professor at the
25	University of Lyon in France, but now he's a

1	director at Syngenta, which is an agrichemical
2	company. And Cian Kingston works at another one of
3	my companies called Vividion in San Diego.
4	Q And which of these listed authors were
5	affiliated with Bristol-Myers Squibb at the time of
6	this publication?
7	A That would be Michael Schmidt, Bin Zheng,
8	Stephen Mercer, Ivar McDonald, Richard Olson, Ye
9	Zhu, Chao Hang, Jason Zhu, Changxia Yuan, Qinggang
10	Wang, Peter Park, and Martin Eastgate.
11	Q And if you turn to page 3 sorry. If
12	you turn to page 5 of this article, the end of the
13	article, it's not the last page, but it's the
14	penultimate page. There, right here. Yeah.
15	And do you see
16	A This one? This one?
17	Q No, no. Next page. There you go.
18	A This one, okay.
19	Q And if you look at the upper right-hand
20	corner, there's a statement that says, "Competing
21	Interests," and it says, "A provisional U.S. patent
22	application on this work has been filed (application
23	62657551) ."
24	Do you see that?
25	A Yes.

Q And does that refer to the a patent
application related to the patent that the '554
patent that your team won an award for last year?
A Yes, I believe so.
Q Okay. So this was really a joint effort,
the work that was conducted on that relates to
P(V) that's in this article and that's in the '554
patent, was a joint effort between the teams of
Scripps and Bristol-Myers Squibb, right?
A Yes.
Q And your understanding is there are other
articles that were written where you're an author
that relates to this work as well, correct?
A Yes.
MR. SHORES: If we can put up Exhibit
2031, please.
(Exhibit 2031 marked for identification.)
Q And, Dr. Baran, you see this Exhibit 2031?
A Yes, sir.
Q And what is this document have you seen
this document before?
A Yes. I wrote the paper.
Q Okay. What is this document?
A This is referring to the chemistry that we
talked about and the other one of the patent

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1	application you had questioned me on earlier before
2	the break. In this article we're focused mainly on
3	making phosphorus carbon bonds in a stereospecific
4	fashion.
5	Q Okay. So this relates to the work in the
6	patent application that we looked at which was
7	Exhibit 2043; is that right?
8	A I'll assume your exhibit number is right,
9	but yes.
10	MR. SHORES: If we can put that up, just
11	for the record, can we put up Exhibit 2034, please.
12	(Court Reporter clarification.)
13	BY MR. SHORES:
14	Q Okay. So does this confirm your testimony
15	that the work that was done the work that's
16	reflected in the article we reviewed in Exhibit
17	2031, that this patent relates to that work, this
18	patent application relates to that work; is that
19	correct?
20	A Yes, sir.
21	MR. SHORES: So if we can put up Exhibit
22	2032, please actually, can we go back to 2031.
23	Q And here there are a number of authors
24	that are listed, and you're listed as an author,
25	correct?

A Yes.
Q And are there representatives from both
Bristol-Myers and Scripps here?
A Yes, there are.
Q Okay. Is there anything that you disagree
with in this in this article?
A I certainly don't think so.
MR. SHORES: Okay. And if we can put up
Exhibit 2032.
(Exhibit 2032 marked for identification.)
Q Dr. Baran, you recognize this document in
Exhibit 2032?
A Yes, I do.
Q And what is this document?
A It's a paper we published in 2021. I
wrote most of this paper.
Q Does this paper relate to the '554 patent?
A I believe there are aspects of this work
that are encompassed within the '554 patent.
Q If we move to page 6 of this, do you see
where it says "Interests"?
A Yes.
Q It says that those individuals that are
initialed are listed as inventors on U.S. Patent
Application Number 2019/0322694?

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1	A Yes, I see that.
2	Q Okay. Okay. If we go back to the first
3	page. And, again, does the listing of authors here
4	represent a combination of members of both Scripps
5	and BMS?
6	A Indeed it does.
7	Q Thank you.
8	And do you disagree with anything that's
9	written in this paper?
10	A I don't think so, no.
11	Q And if we go to Exhibit 2033.
12	(Exhibit 2033 marked for identification.)
13	Q Do you recognize this document, Dr. Baran?
14	A Yes, sir.
15	Q What is this document?
16	A This is like a perspective review article
17	that we wrote to kind of summarize this emerging
18	area that we were working on.
19	Q And when you say "we were working on," who
20	was who is "we"?
21	A "We" is the primarily the Scripps team,
22	but jointly, of course, with Bristol-Myers Squibb.
23	Q Okay. If we move if you go to page
24	1482, which is the legend on the bottom.
25	Do you see that? Do you see where it says

1	"Corresponding Author"?
2	A Yes.
3	Q And you see where it says "Phil S. Baran -
4	Elsie Biotechnologies"?
5	A Yes.
6	Q So was this paper written on behalf of
7	while you were, I guess, wearing your Elsie hat or
8	wearing your Scripps hat?
9	A Both, both addresses are given.
10	Q And this is dated September 10th, 2021,
11	correct?
12	A Correct.
13	Q And the prior exhibit, Exhibit 2032, is
14	also dated September 10th, 2021, right?
15	You have to go back
16	A Correct.
17	Q So it seems that there are two papers that
18	were published on the same day; one indicates that
19	an affiliation with your affiliation with
20	Scripps, and the other reflects your affiliation
21	with Elsie, right?
22	A No.
23	Q Okay. Help me understand.
24	A Okay. If you look at the corresponding
25	author details, it says both Elsie and Scripps

1	there. So that la the because it la a review
	there. So that's the because it's a review
2	article, I put both affiliations.
3	Q And do you recall the circumstances
4	surrounding when these were published?
5	They were published on the same day. Are
6	they do they relate to the same subject matter?
7	A Very yeah, the point of having this
8	come out on the same day was the science paper was a
9	big breakthrough, and this review was held in the
10	galley stage until that paper came out so that
11	people would have a broad perspective of where the
12	science paper fell into the entire field as a whole.
13	This is a review. So there's no new
14	primary data in this paper. It's just a review.
15	Q Okay. Does Elsie and Scripps have a
16	contractual relationship?
17	A Scripps has equity in Elsie.
18	Q Okay. Is there is there let me ask
19	you this. So how was Elsie formed? What's the
20	background on the formation of Elsie?
21	A So that's a fun story. How far back do
22	you want me to go?
23	Q From the beginning, if you can.
24	A Okay. So the student Kyle Knouse, who was
25	working on this who was the primary graduate

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1	student working on P(V) chemistry in my lab, started
2	collaborating with a student in Phil Dawson's lab by
3	the name of Dillon Flood. That was, maybe, in
4	2020-ish time frame, during COVID. And they were
5	both on the same track to graduating at a relatively
6	similar time.
7	And all graduate students are faced with
8	this existential question of what to do in their
9	future career; do they do a post-doc, do they do
10	go to industry, do they go into consulting, patent
11	law. So many different cool career options they can
12	choose. And the two of them decided that the
13	technology they had worked on and collaborated on
14	was profound enough that it would form the basis for
15	a company. And so they decided after they
16	graduated, that they would start Elsie.
17	And then in the meantime, I had been
18	working hard to try to get funding for that company.
19	We were able to identify an investor who put in a
20	seed round that enabled the company to begin. So
21	within a few weeks of their graduation, they had a
22	hood and they had supplies and they had a budget and
23	Elsie was born.
24	Q And the technology that Elsie is founded
25	upon is the P(V) reagent technology, right?

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1	A The initial the initial investor for
2	Elsie was Sorrento Therapeutics.
3	Q Does Elsie so you're saying Elsie
4	in-licenses certain of the P(V) technology?
5	A They obtained nonexclusive license to use
6	and to be able to commercialize, and there are terms
7	associated with that contract.
8	Q Right. And then when you say "commercialize,"
9	what does that mean, like, sell the sell the
10	reagents?
11	A No, we wouldn't sell the reagents.
12	Meaning let's say we used the Elsie platform to
13	identify the very best oligonucleotide therapeutic
14	candidate and it has within it stereopure
15	phosphorothioate linkages. And then the way we
16	would the way we would make such a compound would
17	be using the P(V) sci technology, that is covered in
18	the papers we've all looked at today. And then when
19	a commercialization event happens, let's say it goes
20	all the way to FDA approval, you need a way to make
21	a lot of it. And so we have freedom to operate to
22	use sci to make that material.
23	Does that make sense?
24	Q Yeah. So you're able to use sci in order
25	to synthesize these these oligonucleotides, the

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1	product, the commercial aspect would be the
2	oligonucleotide as a therapeutic?
3	A Exactly.
4	Q But you're allowed to use the reagents
5	internally, but you're not going to be in the
6	business of selling reagents?
7	A Exactly.
8	Q Yeah. So going back to the relationship
9	between Scripps and BMS, what is your understanding
10	of that relationship?
11	When did that when did this
12	relationship when was that relationship forged
13	relating to P(V) chemistry?
14	A Oh, that's another long story. You want
15	it from the beginning?
16	Q Yes, please.
17	A Okay. So more than a decade ago I have
18	been consulting with Bristol-Myers since around
19	around 2005. And around 10 or 10 to 12 years
20	ago, I had the opportunity to pitch or pose to
21	executives at Bristol-Myers the formation of a
22	unique collaboration model between the research
23	institute and the company, Bristol-Myers. And as
24	part of that collaboration, they would work on
25	mutually exciting research projects with a number of

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1	groups at Scripps, our group being one of them.
2	Roughly 2015 or so, Martin Eastgate, who
3	was a continuous collaborator of ours at
4	Bristol-Myers, asked us if we would be interested in
5	working on, you know, a way to fix the
6	stereochemistry problem associated with making
7	stereopure oligonucleotides bearing phosphorothioate
8	linkages.
9	And at that time this was an area that the
10	lab had not we had not been engaged in stereopure
11	oligonucleotide synthesis, so we viewed it as a
12	really cool opportunity to go beyond consulting,
13	just sort of giving out suggestions and actually do
14	something in our lab on this topic.
15	And so we assembled a team and we had
16	every two weeks biweekly meetings, and went back and
17	forth, thousands of experiments, many things didn't
18	work, some things did. It was long trials and
19	tribulations before the ultimate successful outcome
20	that, you know, you see in those various
21	publications.
22	Is there any detail I've missed?
23	Q No. I mean, you've generated a lot of
24	work here, it seems, from you know, based on P(V)
25	chemistry, you know, between the Scripps team and

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1	the BMS team, and there were patents that were
2	generated as a result of that.
3	So I guess one question is: Are you
4	familiar with there being are you familiar with
5	the collaboration agreement are you familiar that
6	there that a collaboration agreement exists
7	between Scripps and BMS?
8	A Oh, of course, yeah.
9	Q Do you have a copy of that?
10	A I do I would have to obtain it. I
11	don't know if it's on my computer right now. But
12	if if Jeremy signs off on that, I'm sure I could
13	as long as Scripps doesn't think Scripps or
14	BMS doesn't think it's like a confidential
15	agreement, then I have no problem with sharing it
16	with anyone. But it's up to Jeremy and Scripps and
17	BMS. I have no idea.
18	MR. EDWARDS: I have no stake or guidance
19	in this, Dr. Baran. You're going to have to
20	determine for yourself whether that agreement is
21	confidential and can be disclosed to third parties,
22	and if so, under what circumstances.
23	There hasn't been a formal request for any
24	discovery in this case other than this deposition.
25	So we would have to go through the correct

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1	procedures and consult with you regarding
2	confidentiality offline. We cannot do that on the
3	fly today.
4	THE WITNESS: Okay.
5	MR. SHORES: Well, I mean, Jeremy, we can
6	maybe talk off record relating to third-party
7	confidentiality. But the you know, this
8	deposition transcript can be marked highly
9	confidential, and then there are procedures in place
10	that would ensure the protection of third party
11	you know, third-party confidential information.
12	And we we would certainly want copies
13	of some of these materials that we're going to be
14	covering and, you know, whether that's through a
15	formal document request or formal processes
16	through the through the PTAB or, you know,
17	through agreement, you know, with petitioner and
18	with these third parties to determine whether they
19	can just provide it to us. But we can talk about
20	that.
21	MR. EDWARDS: Yeah, I mean, for the time
22	being, Dr. Baran needs to use his own judgment and
23	not disclose during this deposition any information
24	that he has reason to believe is confidential
25	regarded as confidential by some third party because

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1	none of those protections are in place at the
2	moment.
3	MR. SHORES: We we are willing to mark
4	this transcript highly confidential. But if you're
5	saying that that's forming the basis for Dr. Baran
6	not to provide testimony whether he believes it's
7	confidential or not, then we will, you know, take
8	issue that we can call the call the Board to get
9	their ruling on that.
10	But unless it's privileged or work
11	product, there's there's really no basis to
12	refuse to provide testimony, especially when we are
13	agreeing to mark the transcript highly confidential.
14	MR. EDWARDS: Well, there's no protective
15	order in place. So marking it confidential doesn't
16	have any context or meaning, absent some prior
17	agreement that gives it meaning, and that prior
18	agreement would be a confidentiality order that's
19	been entered in these proceedings, which has not
20	happened.
21	This is the very first time right now that
22	you are broaching the subject of a protective order,
23	of marking this transcript confidential, of seeking
24	fact discovery, of seeking confidential discovery
25	of confidential materials either of a party or of a

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1	third party. And so I'm not comfortable permitting
2	the witness to testify regarding confidential
3	information absent appropriate protections in place.
4	MR. SHORES: Okay. We can let's flag
5	that to call the Board. I think it's right to speak
6	with the Board about this.
7	MR. EDWARDS: That's fine. You want to do
8	that you want to take a break from the deposition
9	and do that today?
10	MR. SHORES: Yes. I mean, we're getting a
11	second we can come back and conduct another
12	deposition, but that's that's not an option. We
13	need to have this resolved today. And it's not our
14	confidential information to protect, so we wouldn't
15	be moving we wouldn't be a movant for a
16	protective order. That would be on your that
17	would be your call.
18	And the we would we would stipulate
19	to the Board's, you know, standard protective order.
20	But again, we would also mark this transcript highly
21	confidential and subject to the Board's, you know,
22	ruling on the protective order.
23	THE WITNESS: So counsel, if I may,
24	there's nothing to hide. It's a very simple
25	contract. And the only issue is if I had it on my

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1	computer, I would be happy to just show it on the
2	screen and give it to you, it's fine by me.
3	The issue is I could get fired or the
4	contract with BMS could be terminated and I could be
5	in a big lawsuit if I did that without asking the
6	Office of Technology Development and then they have
7	to ask BMS. Like there's a procedure it has to go
8	through.
9	I mean, I can tell you in broad strokes
10	everything I know about the collaboration. But in
11	terms of getting a document like the contract
12	between Scripps and BMS which covers like eight
13	different research groups, I just don't know if I'm
14	allowed to do it without getting you know,
15	without being fired.
16	So, yeah, I'm happy to go through whatever
17	procedure. But it's a fairly simple contract;
18	there's nothing to hide in it.
19	MR. SHORES: Okay. Well, I guess there's
20	two different things, one is the and this is to
21	Jeremy, because I'll talk with Jeremy. We're not
22	looking for the documents sitting here today. What
23	we are looking for is answers to our questions
24	you know, truthful answers to our questions that,
25	you know, whether they're confidential, whether you

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1	deem those answers to be confidential or not, we're
2	entitled to that discovery, and so
3	THE WITNESS: What did I not answer?
4	MR. SHORES: Excuse me?
5	THE WITNESS: What did I I've answered
6	everything. What do you want to know?
7	MR. SHORES: I'm not, with respect, I
8	didn't say
9	THE WITNESS: Okay. Okay.
10	MR. SHORES: I'm saying I will be asking
11	questions and what I'm seeking is testimony, and if
12	you determine that that testimony is confidential,
13	you still must testify to that.
14	MR. EDWARDS: Hang on a second. So, first
15	of all, I lost my feed. Hang on.
16	Okay. I got it back.
17	I think the best next step is for you to
18	be asking the witness if he believes, sitting here
19	today, he is in possession of information that is
20	confidential to some third party. And if the
21	witness is comfortable answering questions and
22	doesn't feel there is some sort of risk of breach of
23	contract along the lines he just described, some
24	breach of confidentiality along the lines he just
25	described, then I am certainly not going to instruct

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1	the witness not to answer if there's nothing
2	confidential of a third party at stake here.
3	So why don't we start by figuring out if
4	there is any risk based on what he thinks he knows.
	-
5	MR. SHORES: Okay. That's fair. We can
6	proceed with in the sense of process, we don't
7	agree with how you know, your characterization of
8	your point of view on that. We believe that, you
9	know, the confidential information is certainly
10	discoverable, and there are procedures in place,
11	both on the trial practice guide, but also, you
12	know, with the marking it highly confidential, but
13	also agreeing to, you know, a protective order such
14	that the third-party confidential information is not
15	disclosed.
16	But let's we'll proceed I'll proceed
17	with questions and we can sort of navigate it that
18	way.
19	How does that sound?
20	MR. EDWARDS: Yeah. And I think for
21	Dr. Baran's benefit, I don't have the underlying
22	facts here, only Dr. Baran does, and only Dr. Baran
23	can figure out for himself if whether he believes
24	the information you're asking him to testify about
25	is confidential to some third party.

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1	So, Dr. Baran, if you if you are asked
2	a question in this deposition that you believe
3	implicates third-party confidentiality concerns,
4	then you should say so. And then then and only
5	then will we have something that I think is ripe in
6	terms of a disagreement on how to proceed between
7	the counsel here.
8	But unless and until you've got some
9	confidential information that you're not comfortable
10	disclosing during this deposition, then we should
11	proceed.
12	MR. SHORES: Okay. Let's proceed. And
13	when I say "okay" it doesn't mean I agree with your
14	statement. It's just we'll proceed with the
15	questioning and we can address these as as, you
16	know, the need arises here.
17	MR. EDWARDS: Okay.
18	BY MR. SHORES:
19	Q So going back to your involvement with
20	Scripps first of all, are you a you're an
21	employee of Scripps, correct?
22	A Correct.
23	Q And you have been an employee of Scripps
24	for how long?
25	A Since 2003.

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1	Q And then the work that Scripps did with
2	Bristol-Myers Squibb, the work that let me back
3	up.
4	You had some consulting relationship with
5	Bristol-Myers Squibb previously, correct?
6	A Yes, dating all the way back to I would
7	say could be wrong, but I believe the consulting
8	with BMS started around November of 2005.
9	Q Okay. And is that consulting did that
10	consulting relationship relate to P(V)?
11	A Not in 2005.
12	Q Was that consulting relationship with you
13	as an individual?
14	A Yes.
15	Q Okay. And what was the compensation of
16	that that consulting relationship with
17	Bristol-Myers?
18	A It fluctuated over time. I believe that a
19	formal exclusive consulting contract was codified in
20	2006, and I believe that the rate was for each
21	day it was about about \$4,000 per day of
22	consulting. I think that was about the right
23	number, but I could be wrong. It's around that
24	ballpark.
25	And each day of consulting would be eight

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1	hours of meetings, along with, you know, usually
2	dozens, if not hundreds of pre-read questions that I
3	would prepare for in the pre-COVID days before Zoom.
4	So, you know, lots of preparation with paper and
5	staying up all night on the red-eye flight preparing
6	the questions and answers to it.
7	And then the visits would be anywhere from
8	two or three days, sometimes a fourth day if there
9	was another site that they wanted me to go to. And
10	with each day, there was a bunch of pre-read
11	questions to address.
12	That's generally how how it works with
13	them. Now, these days, I don't have to travel. I
14	can do everything over Zoom.
15	Q And where are you traveling to during this
16	work with BMS in the 2005 time frame?
17	A Until around 2018, '19 is when things
18	became more virtual, WebEx, Teams, Zoom. Until that
19	period it was visiting their Connecticut site now
20	there's no more Connecticut site, but there was a
21	Connecticut site and New Jersey site. There was a
22	couple of New Jersey sites; one was Lawrenceville,
23	one was Hopewell, and another one was New Brunswick
24	which was a process site.
25	And then there were a couple of occasions

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1	where I had to visit their San Francisco site, and
2	there were a couple of occasions where I had to
3	visit their newly-opened at the time their
4	newly-opened Cambridge, Massachusetts site.
5	Q Okay. And then do you still have a
6	individual consulting relationship with BMS?
7	A Oh, yes, mm-hmm.
8	Q Okay. And have you ever worked with BMS
9	as an individual on projects relating to P(V)
10	chemistry?
11	A As an individual. The lines are blurry.
12	So sometimes there would be consulting questions
13	related to it. But that was usually encompassed
14	within the collaboration with Scripps. And 99
15	percent of the consulting questions that I would get
16	as part of my individual consulting relationship
17	with the company pertained to issues of medicinal
18	chemistry, how to make a certain type of molecule,
19	the molecule could be a small molecule, it could be
20	a peptide, it could be a cyclic dinucleotide, it
21	could be oligonucleotide, it could be an antibody
22	drug conjugate. Anything you can imagine they work
23	on, that could be encompassed within the scope of
24	the types of questions I get routinely.
25	Q So did any of the consulting you've done
1	with BMS from the beginning 2005 time frame until
----	--
2	today involve P(V) chemistry?
3	A It's hard to say for me to parse out what
4	umbrella that would be under because the
5	relationship with them is so close. As I said, like
6	10 or 12 years ago, we started collaborating our
7	group and five or six other groups at Scripps,
8	academic groups at Scripps started collaborating
9	with them.
10	So sometimes I would get an email on a
11	question relating to P(III) or P(V), and as part of
12	my agreement with them, I answered their questions
13	to the best of my ability without regards to what
14	hat I'm wearing; am I wearing the hat of
15	collaborator that does research together or am I
16	wearing the hat of, you, know individual consultant.
17	Does that make sense? Because we're
18	super we have almost 20 years together. So I
19	take questions almost every every few days. Just
20	this weekend I got another question from them
21	randomly you know, they have hundreds of chemists
22	and they're welcome to email me any time with any of
23	their problems.
24	Q And is there who do you work with
25	primarily or who do you interact with primarily at

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1	BMS?
2	A I interact with dozens of chemists there.
3	I mean, if you're asking who is like the person in
4	charge of consulting, is that the question?
5	Q Sure.
6	A So on the process side, the person who
7	primarily sends me my package for official
8	consulting business, the next one I think is next
9	week, would be Mike Schmidt, who is actually on the
10	screen right now. He's like in charge of consulting
11	relationships.
12	So for process chemistry, he'll get, you
13	know, all the teams together and say what questions
14	do we have for Phil, he's coming in a couple of
15	weeks. He puts a package together and sends out a
16	package with all the questions.
17	And then for the New Jersey sites, it's
18	Jeremy Richter. That's Jeremy, and then same as my
19	counsel spelled, and then the last name is
20	R-i-c-h-t-e-r. That's the current person who gets
21	the questions together for New Jersey.
22	For San Diego it's a mixture of various
23	people. And he and these people change over the
24	years. So they are the first people that are
25	currently in charge of sending those questions, but

1	over the years there is turnover and different
2	people are in charge of getting me those packages of
3	questions.
4	Q And you said you have a consulting
5	agreement with BMS and with BMS, correct, you as
6	an individual?
7	A Correct. Correct.
8	Q Do you have a copy of that document?
9	A My admin probably does. I I personally
10	have no problem with you having that document. I
11	mean, but I don't know where it is on my computer
12	now. And we can take a break, I can email my admin.
13	But after this deposition is over, I'm
14	happy to have Shelly find it and send it to you. I
15	don't see why it would be certainly there's
16	nothing in there that for me is confidential.
17	Q Are there any other is there a single
18	agreement or are there multiple consulting
19	agreements that you individually have with BMS?
20	A I mean, over the years it's basically the
21	same consulting agreement, but just the change of
22	date, and I think they increased the rate for
23	inflation over the years. But there's no, you know,
24	there's no big change over the years in the
25	consulting agreement.

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1 Q Okay. Do you own shares in BMS 2 individually? I might through an ETF or Fidelity or 3 Α 4 something like that. But, you know, in my private, 5 you know, accounts, not to my knowledge. 6 That wasn't part of your arrangement with Ο 7 BMS? 8 Α No. 9 All right. If we now go over to Scripps, 0 10 in the work that Scripps conducted with BMS that 11 generated this IP that, you know, based on P(V) 12 chemistry --13 А Yes. -- you testified earlier that there is a 14 Q 15 collaboration agreement between the Scripps and BMS, 16 as would be expected, right? 17 Correct. Α 18 Okay. Do you know if BMS sells P(V) 0 19 reagents? 20 А They do not. You know that for certain? 21 Ο 22 А Yes. 23 0 And do you know if BMS has collaborated with another party in order to sell P(V) reagents? 24 25 I believe they have an agreement with Α

1	Sigma-Aldrich, which is now I think owned by Merck
2	KJA, but it's known I think it's known as
3	MilliporeSigma. They keep changing the name. But
4	they have an agreement with MilliporeSigma,
5	Sigma-Aldrich, whatever it whatever it's called,
6	to be able to sell those reagents for research
7	purposes only, clearly defined as research purpose
8	only.
9	Q Your testimony is that MilliporeSigma
10	sells the P(V) reagents for research purposes only?
11	A Correct.
12	Q And how do you know that?
13	A I think that's that was part of the
14	contract that they negotiated with them, is that it
15	would be research purpose only. I mean, the intent,
16	of course, is that BMS very much wants the world to
17	be able to use these reagents because they think
18	they're useful. But if someone wanted to, let's
19	say, make a commercial product using these reagents,
20	then they would have to go talk to BMS and discuss
21	licensing terms.
22	Q Okay. And to your knowledge, has BMS
23	to your knowledge, have any of these P(V) reagents
24	been sold for research purposes?
25	A I believe, yeah, they sell a lot.

1	Q When you say "a lot," how much is that?
2	A I don't know. But all I know is that I
3	think Sigma always has a hard time keeping up with
4	the demand and the stock and so I'm assuming they
5	sell well.
6	Q And
7	A And I also can glean that from the patents
8	that are out there from other companies like Wave,
9	Roche, others there's other companies out there
10	that have used sci in their patents. So I'm
11	assuming they either made it or they purchase it
12	from Sigma-Aldrich.
13	So they're all just speculations and
14	assumptions. I don't have like an Excel spreadsheet
15	with sales numbers.
16	Q Right. Right. Thank you.
17	The patents, they are jointly owned,
18	right?
19	I mean Scripps and BMS jointly own the
20	for example, the '554 patent we were referring to
21	looking at earlier, right?
22	A I believe that's correct, but I could be
23	wrong when it gets into law like this. It might be
24	that that BMS purchased all the rights. I don't
25	that I'm not I'm not a hundred percent sure on

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1	that. I think they are jointly owned, but it's over
2	my head in terms of the legal ramifications of who
3	owns what.
4	Q So in terms of Scripps' deal with BMS,
5	does Scripps receive a revenue stream from BMS based
6	on the sales of P(V) reagents?
7	A I have no idea. I don't I don't I
8	have not gotten any personal compensation from the
9	sale of those reagents. I don't know if you
10	know, reagent business is not a generally, you know,
11	the kind of market that BMS generally cares about
12	because it's very low, low margins and low level
13	revenue. Big pharma is interested in billion dollar
14	things, not in a million here, a million there.
15	So I don't know what Scripps gets, if
16	anything, or how much BMS has gotten from the sale.
17	I don't think they care at all what they make from
18	the reagents. The point is not to make money from
19	the reagents.
20	Q When you say "the point is not to make
21	money from the reagents"
22	A No.
23	Q is that also true for BMS?
24	A Yeah, all the scientists I talked to
25	there, they will admit all of them will say, you

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1	know, whatever amount you make from a reagent sale
2	is not what's important.
3	I think where they could recoup their
4	investment is a few things. Number one, using it in
5	their own portfolio to which they have, to save
6	themselves millions of dollars in things like
7	manufacturing, saving their medicinal chemists time.
8	So they've saved a lot of money and time using these
9	reagents for their own personal purpose.
10	And then in the future, maybe there will
11	be a company that has a therapeutic where the best
12	way to make it is using those reagents, and then
13	they'll go to BMS and say, hey, we would like to
14	make our product and we want to use this reagent,
15	can you give us some terms so that we can license it
16	for our product. And then there will be another
17	that would be a significant probably financial event
18	for them.
19	Q But isn't that speculation, though,
20	Doctor, that, you know, knowing what BMS's business
21	model is relative to these reagents?
22	A What's the question? Isn't that what?
23	Q Isn't that speculation, your testimony
24	relating to what, you know, commercial value BMS
25	sees in these reagents?

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1	A Well, it's not I wouldn't put it in the
2	speculation category just because I've talked to the
3	people in BD and all the scientists at BMS and their
4	opinion is very in line with what I've just stated.
5	Q And you don't have firsthand knowledge
6	in other words, you're not making commercial
7	decisions for BMS, right?
8	A Of course, no.
9	Q And then when we talk about
10	MilliporeSigma so you testified BMS is a
11	really they're focused on therapeutics, right?
12	A Correct.
13	Q For their commercial model?
14	A Correct.
15	Q And MilliporeSigma, going back, you talked
16	about there is a deal between BMS and MilliporeSigma
17	to commercialize the P(V) reagents, right?
18	A Correct.
19	Q And are you familiar with what the terms
20	of that deal is vis-a-vis
21	A No.
22	Q BMS and MilliporeSigma?
23	A No, I do not know.
24	Q With respect to the agreement between
25	Scripps and BMS, do you stand to make any to gain

1	any financial revenues based on sales of P(V)
2	reagents?
3	A Not to my knowledge. I mean, they have
4	been on sale for a long time. I'm not aware of
5	getting any kickback or payment for them.
6	Q A lot of institutions, like for Harvard
7	University across the river here or MIT, their, you
8	know, professors stand to gain a percentage of
9	royalties that are generated from the
10	commercialization of patents and technology that
11	they were an inventor on, and those are publicly
12	available.
13	For example, if you went on to Harvard's
14	website or MIT's website, you would see how that
15	how that works.
16	And so could you please describe the
17	process at Scripps the question is, do you
18	would you stand to receive any financial
19	compensation based on royalties received on the P(V)
20	project with BMS?
21	A I don't know. I don't think so. I mean,
22	I haven't I haven't received anything. So I
23	don't the nature of this contract with with
24	BMS I think allows them to kind of take ownership of
25	this aspect of it. And I'm to my knowledge, I

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1	don't get any, you know, financial gain from, you
2	know, the whatever, you know, trivial amount of
3	money that Sigma makes from selling these reagents,
4	not to my knowledge.
5	But, again, I'm, you know, happy to share
6	whatever contracts there are, share it. Who knows,
7	maybe you'll find something and I can knock on
8	Scripps' door and say, hey, you owe me a couple
9	thousand bucks, so you may be doing me a favor.
10	Q But when you say trivial amount of money
11	that MilliporeSigma makes from the reagents, what do
12	you mean by "trivial"? Like do you have an amount
13	of
14	A Well
15	(Simultaneous speaking.)
16	(Court Reporter clarification.)
17	Q Yeah. Okay. The question is whether
18	Dr. Baran is aware of the amount of sales that
19	the amount of P(V) reagent sales that MilliporeSigma
20	has made to date.
21	A I don't know that. But what I can say is
22	that it's not my first time being involved in
23	reagent sales. There was another instance with a
24	reagent we developed with Pfizer, having nothing to
25	do with oligonucleotides or the subject matter of

1	this case, and there was a whole suite of reagents
2	that were commercialized, I think they sold millions
3	of dollars of reagent.
4	I think there was a check for like a
5	thousand bucks or something that came back to me
6	personally. It was like, you know, after taxes, you
7	don't even know it happened kind of thing, and
8	that's because the margins on these reagents are
9	generally low.
10	So no one in academia, with very few
11	exceptions, I know of a couple of exceptions but
12	no one, you know, invents a reagent to get rich.
13	It's not, you know, if you would like to make money,
14	you invent a drug, you start a company, you have a
15	liquidation event, that kind of thing. Selling a
16	reagent is like a lemonade stand.
17	Q Do you have an employment agreement in
18	place with Scripps?
19	A Of course.
20	Q Okay. Do you have a copy of that?
21	A Somewhere, but Shelly is the best person
22	to get it from and I'm happy to provide all of that,
23	of course.
24	Q So we talked earlier you were saying that
25	you haven't received any funds relating to the sales

1	of P(V) reagents through this collaboration with
2	BMS. But my question is whether you're entitled to
3	receive payments?
4	A I honestly don't know. I never even asked
5	because, like, reagents are not it's not a place
6	to try to earn money for an academic group, you
7	know.
8	Obviously the people in this case, Hongene
9	and ChemGenes and all the people who sell reagents,
10	if you sell a million reagents, you can do the math,
11	you don't need very high margins and you can have a
12	good company.
13	But if you're an academic and you invent a
14	reagent or two, you know, that's the point is
15	stimulating the driving force or the impetus for an
16	academic to work on a new reagent is not to make
17	money. It's to do something useful for society that
18	people will use. And, you know, it's kind of like
19	an academic credential, like, look, we have a
20	reagent that people care about, can use, solve
21	problems, there's a dying cancer patient that
22	benefited in a very early stage from this reagent.
23	You know what I mean? That's the value we
24	get. Not, oh, I made \$500 extra.
25	Q With respect to Scripps and Elsie, you

1	testified earlier that really Elsie is it fair to
2	
	say Elsie is a spinout of Scripps?
3	A I mean, you could look at it that way
4	because the four co-founders are all from Scripps.
5	Scripps owns a good amount of equity in the company.
6	So, yeah, you could call it I wouldn't be against
7	you calling it a spinout. That would be an accurate
8	because all the founders are from Scripps, yeah.
9	And the technology, some of it was
10	invented at Scripps. But as I mentioned before, the
11	main proprietary thing that's at Elsie right now
12	that's generating revenue did not originate from
13	Scripps. But the people who are employed there, the
14	four co-founders, yeah, those are Scripps-educated
15	folks.
16	Q And how many shares do you own in Elsie?
17	A Oh, I don't know the number of shares.
18	It's around, I think, around 3 million or so.
19	Q And what percentage of ownership do you
20	have in Elsie?
21	A I think it's about 10 percent.
22	Q Who is the majority owner in Elsie? Is
23	that Sorrento?
24	A It's not Sorrento anymore. So Sorrento
25	went bankrupt, and they owned 36 percent of the

1	charge and it was required and by a separate semanny
	shares, and it was repurchased by a separate company
2	in bankruptcy court. And so the majority
3	shareholder at this point, it's probably employees
4	and this other investor company called Awen,
5	A-w-e-n, Biosciences. But I think the majority is
6	probably all the co-founders, I think.
7	Q Does BMS have an equity interest in Elsie?
8	A They do. They do, yes.
9	Q What amount is that?
10	A I think it's around 4 or 5 percent, but
11	don't hold me to it.
12	Q And then your testimony is that Elsie
13	in-licenses the P(V) technology developed between
14	Scripps and BMS, correct?
15	A They have I don't know if "in-license"
16	is the is the word. Maybe it is. But
17	practically speaking, they have nonexclusive rights
18	to commercialize any product using the P(V)
19	technology, and then along with that, there are
20	various royalties and other things that have to be
21	paid. I don't have that contract in front of me.
22	But there are strings attached.
23	Q And that's a direct agreement between
24	Elsie and BMS, correct?
25	A Correct. Correct.

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1	Q And you have a copy of that agreement?
2	A It's probably something that I can get
3	from Elsie. Shelly has everything, I'm sure. And,
4	you know, I don't know if I'm allowed to, but I'll
5	certainly say, hey, you know, can I share this and
6	see if we need to do a confidentiality agreement or
7	whatever Jeremy recommends. But me personally, if I
8	had the document, I would screen share it right now.
9	I don't care.
10	Q And going back to Elsie's Elsie's, I
11	guess, business model
12	A Yes.
13	Q Elsie has a collaboration with Glaxo,
14	correct?
15	A Correct.
16	Q What is the nature of that agreement or
17	that relationship?
18	A Well, it's a collaboration agreement to
19	to benchmark the fidelity and performance of the
20	platform that I mentioned before that was developed
21	at Elsie. So that collaboration doesn't really have
22	anything to do with P(V) chemistry.
23	Q That collaboration, the collaboration
24	between Elsie and Glaxo, doesn't have anything to do
25	with P(V) chemistry?

1	A No.
2	MR. SHORES: Could we please put up
3	Exhibit 2039.
4	(Exhibit 2039 marked for identification.)
5	Q Dr. Baran, do you see this document?
6	A Mm-hmm.
7	Q Have you seen it before?
8	A Yes.
9	Q Okay. What is this document which is
10	Exhibit 2039?
11	A This is a press release, which is kind of
12	like, you know, a way to get excitement in the
13	community about the company. But and I see it
14	says P(V) here, but the nature of what we did with
15	them, there is nothing at this stage of the
16	collaboration maybe in the future, but what we
17	did with them in order to get to a point where they
18	want to trigger, you know, a follow-up, had nothing
19	to do with $P(V)$. Maybe in the future it will, and I
20	think the future is commercialization, you know,
21	moving in that direction.
22	But in the first instance, the
23	collaboration as it is, all the things we did for
24	them so far to get to that proof of concept stage
25	that satisfied what they wanted to see, no P(V)

1	chemistry was used to get to that inflection point.
2	Q But based on this, which is from July of
3	last year, doesn't this indicate that there's a
4	collaboration with GSK and Elsie relating to P(V)?
5	A It says that. But operationally, what
6	we've done so far, there is no P(V) yet. Maybe
7	soon, but not yet.
8	Q I mean, look at your quote here, where it
9	says, "Phil Baran Ph.D., co-founder Elsie
10	Biotechnologies said, 'By leveraging all the tools
11	across Elsie's platform, we can explore the entire
12	chemical oligonucleotide space and uniquely define
13	inter-nucleotide linkages and stereochemistry to
14	tune safety, activity, and delivery of
15	oligonucleotide therapeutics.'"
16	Did I read that correctly?
17	A You did.
18	Q What did you mean and this is
19	what what did you and this is a quote by you,
20	this is an accurate quote from you; is that correct?
21	A Mm-hmm, yup.
22	Q So when you say "leveraging all the tools
23	across Elsie's platform," what is Elsie's platform?
24	A Elsie's platform has got three main tools.
25	The first tool is what we call Rosalind, and

1	Rosalind is the proprietary high throughput method
2	for determining what the optimum sequence is for
3	candidate oligonucleotide, without using
4	bioinformatics or in silico design, we have a way of
5	doing this high throughput to come up with the very
6	best optimum sequence.
7	And then after that downstream would be
8	fine-tuning things like stereochemistry, that would
9	be the $P(V)$ platform. And then after that would be
10	what we call the denote platform, which allows for
11	conjugation.
12	Now, this document was meant to generate
13	enthusiasm in the community, as all small companies
14	try to do to get more collaboration set up. So it
15	is true that Elsie has three legs to its platform;
16	one is Rosalind, one is the P(V) chemistry, and one
17	is denote.
18	However, what we did with GSK so far has
19	not been P(V) chemistry. It has been, so far, only
20	the Rosalind platform, and that's what has generated
21	revenue thus far.
22	Now, moving forward, I think the next
23	stage will probably be indeed to start using P(V)
24	chemistry for sure. That's stage 2.
25	Q When you say there was revenue generated,

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1	approximately how much revenue was generated from
2	A That is that I can't say because I
3	would get in trouble. So that's one you would have
4	to do whatever CDA, contact Elsie because that's
5	we don't tell anybody that.
6	Q And there's you're aware of the
7	existence of an agreement between Elsie and Glaxo?
8	A Yes.
9	(Simultaneous speaking.)
10	Q a collaboration?
11	(Court Reporter clarification.)
12	Q And do you have a copy of that document?
13	A Not on my computer. Again, you can get it
14	from Elsie, if they agree to whatever a CDA or
15	whatever it is that the lawyers need to work on.
16	Q So this high throughput growth high
17	throughput platform, is that software-related or is
18	it
19	A No. Okay. There is a software component
20	because you have a lot of data that you need to
21	analyze. But unlike the traditional way of
22	discovering an oligonucleotide, let's say, an
23	antisense oligonucleotide, where it's only
24	computation, this is experimental results that are
25	then fed into a software algorithm to deconvolute

1	what the data means and turn it into something.
2	But it's empirically derived, not
3	in silico derived. Does that make sense?
4	Q Thank you.
5	So when you talked about the second, you
6	know, leg of the stool or, you know, relates to P(V)
7	chemistry, correct?
8	A Yes, correct.
9	Q If if GSK wants to take the next step
10	and license P(V) technology from you, what what
11	is that what would they use it for?
12	What would you be giving them and what
13	would they be giving you?
14	A Well, that's a nuanced question. It's
15	something that we talk about as a business every
16	day. What would we be giving them. Well, we give
17	them a lot of know-how, a lot of proprietary
18	knowledge on how and when to employ it. We would
19	give them access to the license that we negotiated
20	with BMS to be able to commercialize products that
21	use P(V).
22	What would they be giving us? Well,
23	obviously, you need capital to make things happen,
24	so they would be providing capital. They would be
25	providing know-how. And most importantly, they

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1	would be providing an avenue through the incredible
2	infrastructure and really talented scientists at GSK
3	to take this vision and turn it into lifesaving
4	treatments for individuals.
5	Q But Elsie wouldn't be like a supplier of
6	these P(V) reagents, right?
7	A No. No, Elsie is not a reagent company.
8	That's small beans. No offense to the parties
9	involved here, but that's not our business model.
10	Q And if Glaxo, you know, is it fair to say
11	the more P(V) reagents that Glaxo uses, the higher
12	the financial reward is to Elsie?
13	A No, no. Like I said, if the only thing we
14	had in our platform was the P(V) technology, we
15	would not have a GSK deal. The whole year we spent
16	last year there was nothing to do with $P(V)$, and
17	that's what the agreement was, to field test and see
18	if this platform Rosalind that I mentioned, which is
19	incredible, a large company doesn't just believe a
20	small biotech who says look how amazing this stuff
	Small Dioteen who says look new amazing this stall
21	is and we have many case studies and we said look
21 22	
	is and we have many case studies and we said look
22	is and we have many case studies and we said look how amazing it is, and they're, like, yeah, yeah,

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1	And then we did that last year and it
2	works, and none of the stuff we did has anything to
3	do with P(V) in that first stage.
4	Q If Glaxo were to sell a product that had a
5	P(V) you know, used P(V) or had a P(V) component
6	to it or was, you know, a therapeutic that utilized
7	P(V), would Elsie receive royalties on the sales of
8	those products?
9	A That depends. So, you know, if GSK said,
10	hey, you know, you guys are nice, but we don't want
11	to work with you, we're going to go straight to BMS
12	and just work with them on getting our own license
13	for P(V), then Elsie would not benefit at all.
14	If GSK said we want to work with you
15	because we know that this is much more than P(V)
16	P(V) is like a useful tool. It's like a
17	screwdriver, but there's a difference between a
18	screwdriver and a Ferrari, right? The former is
19	used to make the latter, but the latter has a lot of
20	intrinsic value. And so what they are most
21	interested in is the Ferrari, the platform that does
22	the racing around the track, not the screwdriver
23	which is the later on may be needed for
24	stereopure oligos.
25	So we don't even know at this point

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1	whether the eliges they make eventually and if they
	whether the oligos they make eventually and if they
2	were to continue with Elsie, it's all speculative,
3	whether there would even be a stereochemical
4	component to it. We don't know. It's all
5	speculation.
6	But the reason this collaboration happened
7	and the reason there's enthusiasm currently who
8	knows, in the biotech world tomorrow we might get a
9	call and say we don't want anything to do with you
10	anymore. It's all speculation. Right now they are
11	excited because of the Rosalind platform.
12	Q What is so unique about the Rosalind
13	platform? Why is that
14	A Well well, that's a great question.
15	And we've done pitch after pitch over the years to
16	try to explain this to people.
17	The succinct answer is to think about the
18	way small molecule drugs are discovered and
19	developed, and to think about the way
20	oligonucleotides are developed. Specifically, let's
21	use as a case study, let's use an antisense
22	oligonucleotide. So a small molecule drug is
23	developed by using a lot of structural information,
24	structural activity relationships, binding to an
25	enzyme pocket, making recursive decisions based on

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1	subsequent chemical modifications of a scaffold,
2	optimizing for efficacy, PK, solubility,
3	tolerability, until you finally are able to say
4	there's my API, I can formulate it into a drug.
5	Now, if you think of an antisense
6	oligonucleotide, the first step is not based on a
7	structural finding and finding of an enzyme
8	possibility. It is based upon looking at an mRNA
9	transcript that you would like to bind and then
10	using in silico software for the software to guess
11	for you, well, try this sequence. Maybe this one is
12	good. Try this one. Try that one. You make a
13	bunch of them, you find one that's okay, good, and
14	you proceed forward.
15	The revolutionary advance of the Rosalind
16	platform is that we make hundreds of thousands of
17	compounds candidate antisense oligonucleotides, and
18	we screen those hundreds of thousands of compounds
19	across the entire mRNA transcript in realtime.
20	Because mRNA is like a moving creature, it's moving.
21	It's not a frozen chicken; it's moving. So you can
22	do a direct assay of hundreds of thousands of
23	constructs within the confines, within the context
24	of the moving mRNA.
25	And using the deconvolution, tagging, and

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1	software algorithm that the data the data is fed
2	into, it gives you candidate oligos that are super
3	potent and have unique binding sites that would not
4	be predicted through a bioinformatic regime.
5	So in that sense, it's very similar to the
6	way a small molecule is developed. Because a small
7	molecule, like Lipitor or Prozac, or whatever
8	medicine you know, they don't invent it with a
9	computer. A computer can assist something, but it's
10	not invented with a computer.
11	So does that make sense?
12	Q Yeah, I follow what you're saying.
13	A Okay. Great.
14	Q I go back to an earlier question which is
15	I'm not sure I got a complete answer, and that's
16	not a criticism. But it's if Glaxo develops a
17	therapeutic that utilizes P(V) chemistry, is that
18	you know, will Elsie, under its current arrangement
19	with GSK, stand to gain from that financially?
20	A If the the lead is discovered in
21	collaboration with Elsie and they decide, number
22	one, their lead is discovered with the Rosalind
23	platform, and number 2, there is a $P(V)$ element in
24	there that they decide to work with Elsie to to commercialize,
25	then yes, of course.

1	Q And then if a product is, you know, goes
2	commercial, if, you know, an oligonucleotide
3	product, therapeutic goes commercial, then a
4	significant amount of P(V) reagents would be needed
5	in order to synthesize a commercial product,
6	correct?
7	A It depends. I mean, the
8	oligonucleotide let's imagine, if we're going to
9	do hypotheticals and speculation, let's say they
10	settle on a 16-mer gapmer. And in that gapmer there
11	are two phosphorothioate linkages, with only two
12	linkages, you don't need much reagent to get those
13	two linkages. And so they probably won't need a lot
14	of it, but they will still need a freedom to
15	operate, and that's what Elsie provides.
16	Now, if they have a 20-mer and every
17	single linkage requires P(V), a lot more reagent is
18	needed.
19	Does that make sense?
20	Q Yes, it does.
21	And so if there's but my question is
22	relative to the current arrangement between Elsie
23	and Glaxo, if that were to occur and they would need
24	a license to the P(V) from Elsie, does Elsie stand
25	to receive financial gain from that?

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1	A Of course, sure.
2	Q And similarly with the relationship
3	between Elsie and BMS, that's a different
4	relationship, though, right?
5	A Elsie owns BMS owns 4 or 5 percent of
6	the company equity. They also, I believe, have some
7	terms that give them some royalty stream of any
8	product that uses $P(V)$ in the construction of a
9	commercial product. So BMS definitely stands to
10	gain in any big financial, you know, windfall event
11	for the company.
12	Q When you say "the company," you mean
13	Elsie?
14	A Correct, yes.
15	MR. SHORES: Okay. Maybe take a
16	five-minute break.
17	THE WITNESS: Sure.
18	MR. EDWARDS: That's fine.
19	(Recess 10:33 a.m 10:42 a.m.)
20	BY MR. SHORES:
21	Q Dr. Baran, you're also a co-founder of
22	polyARNA; is that correct?
23	A Yeah. And they have changed their name
24	recently, they are still in stealth, but they have
25	changed their name.

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1	Q Okay. What's the name changed to?
2	A The new name is Convergents Therapeutics.
3	Q Okay. And then when was polyARNA founded?
4	A Well, it was ideated and seeded about two
5	years ago, and then another influx of capital came
6	in from a few VCs roughly six months ago, and now
7	it's operating in stealth. And we anticipate
8	emerging from stealth at the end of the year,
9	meaning we announce our existence to the world.
10	Q Right. Right. And who are the who are
11	the lead investors for polyARNA?
12	A Currently it is NewPath is one, Google
13	Ventures, another one, and Arch.
14	Q Are there any pharma companies that have
15	ownership in polyARNA?
16	A No.
17	Q What is polyARNA's platform?
18	A The convergence platform is, broadly
19	speaking, a new generation of mRNA medicines.
20	Q Does polyARNA utilize P(V) chemistry
21	A They do P(III), P(V), everything, mm-hmm.
22	Q How does polyARNA utilize P(V) chemistry?
23	A Well, without revealing like, you know,
24	confidential details, in some cases stereochemistry
25	matters a lot in certain parts of mRNA, and that can

1	
1	be the cap or the body or the tail.
2	So when we incorporate stereochemistry in
3	certain parts of the mRNA, we're making various
4	analogs, we use P(V) to put the stereochemistry in
5	just because it's the best way.
6	Q It's better than P(III)
7	A Well, P(III), there aren't really any good
8	ways to use P(III) to put stereochemistry. And I
9	know your colleagues here probably would object, but
10	the Wave technology that is out there using P(III)
11	to incorporate stereopure phosphorothioates, the
12	dirty secret of that chemistry is that it
13	stereo-enriched, not stereopure. And further, it is
14	encumbered by IP that is owned by Wave.
15	And so to avoid all that, the chemical
16	problem of needing stereopure and not
17	stereo-enriched
18	(Court Reporter clarification.)
19	A To avoid stereo chemical problems and to
20	avoid IP issues, they use P(V) instead for research
21	purposes.
22	Q When you say the "stereopure," you're
23	talking about the phosphorothioates, right?
24	A Correct.
25	Q And what do you mean by that?

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1	A Well, in mRNA, which is a big oligo, much
2	bigger than an antisense oligonucleotide, some of
3	the internucleotide bonds, you might want to make
4	them phosphorothioate instead of phosphodiester, so
5	that's what I mean.
6	Q Okay. But can't you use P(III)
7	phosphoramidites to make phosphoro
8	phosphorothioates? Excuse me.
9	A You can and we do. The problem is it
10	gives a mixture of the two isomers.
11	Q So it's like a racemic mixture?
12	A Well, racemic is
13	(Technical interruption.)
14	THE WITNESS: Uh-oh. The recording
15	stopped.
16	MR. SHORES: Looks like we lost our
17	technician.
18	(Recess 10:47 a.m 10:48 a.m.)
19	MR. SHORES: Can you read the last
20	question, if there was a pending question.
21	(The following is read by the Court
22	Reporter:
23	"QUESTION: So it's like a racemic
24	mixture?
25	"ANSWER: Well, racemic is")

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1	A Racemic is a word that usually people
2	refer to them as racemic linkages, but technically
3	it's not racemic, because a racemic compound is if
4	you have one enantiomer and another enantiomer and
5	you've got both of them in a one-to-one mixture,
6	that would be racemic.
7	These compounds would have a couple of
8	linkages, for example, and if there are mixtures at
9	that phosphorus, we usually refer to them as
10	(Reporter Clarification.)
11	A If, for example, there are more than one
12	phosphorus stereocenter and you have mixtures at
13	both of those phosphorus stereocenters, the correct
14	terminology would be mixtures of diastereomers.
15	However, for the purpose of this
16	deposition and the colloquialism, it's fine if we
17	refer to a phosphorus stereochemistry that's not
18	controlled as being racemic, it's fine.
19	Q Okay.
20	MR. SHORES: Maybe this exhibit will help.
21	So can we put up Exhibit 2036, please.
22	(Exhibit 2036 marked for identification.)
23	Q Dr. Baran, do you see this document?
24	A Yes, I do.
25	Q Have you seen it before?

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1	A Chemistry World maybe, probably yeah,
2	probably. I don't remember what it says.
3	Q Okay. If you want to take a minute to
4	flip through. It's only a few pages long.
5	A Yeah, just tell me where you want me to
6	focus.
7	Q This what is this document?
8	A It looks like a some sort of news
9	article in Chemistry World that is highlighting one
10	of our papers.
11	Q Relating to P(V) chemistry?
12	A Yeah.
13	Q Okay. If you go to page 2 of this
14	document, there's a figure there. I thought this
15	might be useful to our conversation about the
16	different linkages.
17	Down at the bottom where it says "Native
18	phosphodiesters," do you see that?
19	A Yes.
20	Q Is that the naturally occurring vertebrae
21	that we were referring to earlier?
22	A Vertebrae, internucleotide bond, yes.
23	Mm-hmm, exactly.
24	Q And then if you go all the way up to the
25	top, we see racemic phosphorothioate there, correct?

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1	A Yes. As I said, people often use that
2	term, and if it's referring to the actual
3	phosphorus, you can it's fine to say racemic, as
4	I said.
5	Q Yeah, understood.
6	And then you described would you mind
7	describing the following three internucleotide
8	linkages?
9	A So the next one down is a
10	phosphorothioate, where the phosphorus
11	stereochemistry is defined as being S at phosphorus.
12	The next one is the phosphorus
13	stereochemistry where the phosphorothioate is
14	defined as being R at phosphorus.
15	The next one is an achiral linkage that
16	has two sulphurs, and it's known as a
17	phosphorodithioate.
18	And then the final one is the one we
19	talked about before, which is the one found in
20	nature.
21	Q Okay. Can you use or could one use,
22	one ordinary skill in the art use P(III)
23	phosphoramidite chemistry to synthesize an
24	oligonucleotide having a (audio disruption).
25	(Court Reporter clarification.)

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1	Q Okay. So one of ordinary skill in the
2	art, a chemist use P(III) phosphoramidite chemistry
3	to synthesize an oligonucleotide having a native
4	phosphodiester internucleotide linkage?
5	A Of course.
6	Q What about a racemic phosphorothioate
7	linkage?
8	A Of course.
9	Q What about SP phosphorothioate?
10	A Like I said, there is a technology out
11	there that was invented in Tokyo by the Wada Group
12	that was licensed by Wave, and the my contention
13	is that it is generally known that it will deliver
14	stereoenrichment. Some cases will be very high,
15	some cases won't be as high.
16	So will it give you the S
17	phosphorothioate? Yeah. But will it be a hundred
18	percent to the limits of detection? Often no.
19	MR. SHORES: Okay. I'm sorry, someone
20	is yes. Thank you.
21	Q Is there any, you know, like we have these
22	racemic mixtures, and I know with your qualification
23	with your qualification earlier really means
24	here. But both enantiomers or stereoisomers
25	together, is there an advantage of having one of

1	them isolated versus the racemic?
2	A Well, it depends who you ask and it
3	depends what data. I remember many years ago when I
4	started talking about this at oligonucleotide
5	conferences, there would be great debate. And some
6	people at certain companies would say
7	stereochemistry doesn't matter, and some people
8	would give presentations showing data that
9	stereochemistry definitely matters.
10	Now, fast forward a few years, there are a
11	number of publications and there is a number of
12	pieces of data from various companies that point to
13	the fact that stereochemistry can be hugely
14	important on dictating things like efficacy and even
15	physical properties of an oligo with a
16	stereo-defined linkage.
17	So in my opinion, it's context dependent,
18	because you'll find scientists who will say we don't
19	care stereocontrolled, and you'll find scientists
20	who will say, oh, we've got to have it
21	stereocontrolled.
22	Q Okay. So your testimony is that let me
23	go back to let's just talk about P(V).
24	So is it correct to say that P(V) can be
25	used to synthesize any of these internucleotide
	,
----	--
1	linkages?
2	A Any ones on the slide, correct.
3	Q On page 2 of Exhibit 2036, the figure
4	shown there, correct?
5	A Correct, yes.
6	Q And your testimony is that P(III)
7	phosphoramidites can be used to synthesize all of
8	these as well?
9	A They can, with the proviso that I have
10	outlined that often the current technology to make S
11	and P are often not stereopure, they are
12	stereoenriched, which may be good enough for some
13	companies. But for the reason those two papers
14	were accepted in science was that if you want to
15	make a stereopure, meaning to the limits of
16	analytical detection, there's only one isomer there.
17	As of today, the P(V) technology is, if not the
18	best, a really good option.
19	Q And do you feel that P(V) chemistry has
20	significant advantages over P(III) chemistry?
21	A It can.
22	Q And does that have to do with the what
23	advantages does it have, P(V) chemistry?
24	A Well, it depends on the context. But on
25	first principles grounds, the $P(V)$ chemistry that we

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1	and BMS collaboratively worked on has the advantage
2	of cutting out some steps from the canonical
3	coupling cycle, removing the redox fluctuation,
4	removing some of the protecting groups, and ensuring
5	that you get homogeneous stereopure product.
6	The other thing that's advantageous is
7	that the P(V)-based reagents are a lot more stable,
8	they are bench stable, moisture stable. So when you
9	order a phosphoramidite from a vendor, they are
10	generally vacuum-sealed bags with the bottle, and,
11	you know, you want to keep them far away from
12	moisture, if you can.
13	The equipment that's been invented to do
14	oligonucleotide synthesis using phosphoramidite is
15	airtight and excludes moisture for that reason.
16	Whereas, with the P(V), it's a little bit more
17	forgiving. That's some of the advantages of $P(V)$.
18	Q And you would agree that the use of
19	oligonucleotides as a therapeutic is a growing
20	growing field?
21	A Based on the data, yes.
22	Q And where do you see this field going in
23	the next, say, five or ten years?
24	A It depends who you ask. Some people think
25	that it's only going to be growing, and some people

1	say exponential growth. Some leaders of large
2	companies think that it's the future. That might be
3	too exaggerated.
4	I mean, my personal opinion, if you're
5	looking for that, is that it will be an important
6	component in the arsenal of modalities that we use
7	to potentially treat certain types of diseases.
8	That's what I can say would be like a non-hyperbole
9	answer to the question.
10	Q And you can use P(V) chemistry for these
11	oligonucleotides, correct?
12	A Correct.
13	Q You can also use them, as you discussed
14	earlier, for much larger molecules including
15	messenger RNA, correct?
16	A Correct.
17	Q Are you familiar with phosphoramidite
18	chemistry being used in connection with synthesizing
19	messenger RNA molecules?
20	A Of course.
21	Q And would you see P(V) chemistry as being
22	a replacement for P(III) chemistry in some of those
23	applications?
24	A Maybe. I mean, you know, my job is to
25	educate students, that's my primary job. And from

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1	the beginning, when I got into this collaboration
2	with BMS, when I gave talks on this topic, it was a
3	very calm thing for me because I don't really have
4	skin in the game. I said at many of these lectures
5	in front of hundreds, if not a thousand people, I
6	personally don't care what the result is. Like, if
7	50 years from now nobody is using P(V), I probably
8	won't be alive, but it won't matter to me. I'm just
9	trying to do something useful, and time will tell if
10	the chemistry is, you know, as robust and useful as
11	the gold standard, which is phosphoramidite.
12	But I'm just proud of the great students
13	I've had, and if this is useful, great. If it turns
14	out not to be so useful, all right, well, we're an
15	academic group, we tried.
16	Q But if P(V) chemistry hockey sticks and
17	becomes a very widespread technology that's used to
18	develop a number of therapeutics, you would stand to
19	financially gain; isn't that correct?
20	A Well, that would only be if if the
21	various companies I'm involved in do well as a
22	consequence of that. Like, I don't know if if we
23	do let's do hypotheticals. If we say random
24	company X needs to use P(V) and they approach
25	Bristol-Myers and they say here's, you know, \$10

1	million for up to be able to use $P(M)$ to make our
	million for us to be able to use P(V) to make our
2	oligonucleotide, I don't know if I get any of that
3	\$10 million or it just goes to BMS. I don't think I
4	get any of it.
5	So I would personally financially benefit
6	if Elsie does well, if Convergence Therapeutics does
7	well. You know, that's the I think that's where,
8	you know, my conflict of interest or individual
9	ability to profit comes from.
10	Q Let's go back to polyARNA. I just want to
11	close out that, you know, questions surrounding it.
12	What is your role at polyARNA I'm sorry
13	Convergence Therapeutics pre-stealth?
14	A I'm a co-founder and consultant.
15	Q Okay. Do you serve in any executive role
16	there?
17	A Scripps doesn't allow me to. I'm not
18	legally allowed to be an executive or anything
19	beyond a consultant and a co-founder in any company.
20	Q Does polyARNA have any agreement with
21	Scripps?
22	A Does no.
23	Q Does polyARNA in-license or license any of
24	the P(V) technology that you generated with BMS at
25	Scripps?

1	A As of today, no.
2	Q How does polyARNA use P(V) reagents in its
3	program?
4	
	A To make various analogs of mRNA constructs
5	and test their activity. There's tons of companies
6	that use P(V) chemistry, but as I mentioned, they
7	don't have to pay anything until they get to the
8	point of commercialization. So that could be years
9	from now before, you know, BMS has to engage in a
10	license with any of those companies.
11	They're allowed to use it just by buying
12	the reagent from Sigma or they can have a CRO make
13	the reagent themself. So people are free to use the
14	published work and see where it takes them, if it's
15	useful or not.
16	Q PolyARNA uses phosphoramidite chemistry in
17	its program; is that correct?
18	A Yup, yes, correct.
19	Q And how does it use P(III) phosphoramidite
20	chemistry?
21	A To make various pieces of mRNA that are
22	ligated onto the you know, the body is generally
23	made through in vitro transcription, you know, the
24	body which is, you know, hundreds of oligos long,
25	and then the little tail or the cap might be, you

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1	know, made through phosphoramidite chemistry and
2	then ligated on to the big piece.
3	Q Does polyARNA have any agreements in place
4	with Hongene?
5	A Not to my knowledge. I mean, I think
6	polyARNA buys reagents, as does Elsie, from every
7	vendor out there, including Glen, Hongene, ChemGenes
8	and whatever, Aldrich they just basically, you
9	know, look on SciFinder, see it's available, and if
10	it's a reasonable price, I don't think they pay any
11	attention to who they buy it from.
12	Q So polyARNA, to your knowledge, doesn't
13	have, you know, like a supply contract or anything
14	like that with Hongene or
15	A No.
16	Q or any other kind
17	A No.
18	Q of contract with Hongene?
19	A With any with any supplier, ChemGenes,
20	Glen, whatever, there are no no. They're just,
21	you know, like Bonds or Albertsons, it's where they
22	buy their bread.
23	Q And what about Elsie, does Elsie have a
24	contract with Hongene, to your knowledge?
25	A No. No.

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1	Q No, you mean you know they don't; or you
2	do not to your knowledge?
3	A Not to my knowledge, I don't know of any
4	contract existing between Hongene or ChemGene or
5	Glen, or whatever the suppliers are out there.
6	As far as I know, all of the suppliers are
7	just suppliers. They have a catalog, they buy a
8	reagent from them.
9	Q So in terms of like your time commitment,
10	you're employed by Scripps, you have a consulting
11	relationship with BMS, you're a co-founder at Elsie,
12	you're a co-founder at polyARNA, you're on the
13	scientific advisory of Nutcracker, right?
14	A Yes.
15	Q So in terms of your role at Elsie, are you
16	in any kind of a management role to describe what
17	your time commitment and participation is at Elsie.
18	A I'm a consultant and co-founder. So, for
19	example, we have a weekly leadership meeting that I
20	attend that's about 45 minutes long every Friday.
21	And we have a Slack channel, so the
22	scientists can ping me and say, hey, Phil, we're
23	having a problem with the deprotection of this
24	nucleoside, what conditions do you recommend, or
25	whatever random question they may have. Just like

1	any other company I consult with, they can send me
2	emails and say, hey, we have a problem, can you help
3	solve it, or any of my students, which I'm getting a
4	bunch of Slack messages as this deposition goes on
5	that I'm going to have to answer.
6	So I'm always being pinged on every
7	direction.
8	Q You have as an individual, you have an
9	agreement with Elsie based on your consultancy and
10	also with regard to your stock ownership in Elsie;
11	is that correct?
12	A I believe so, yes, with all of them, I
13	have to for compliance.
14	Q Okay. And you have a copy of that
15	agreement?
16	A Shelly does and I'm sure she can get it to
17	you after this call.
18	Q Okay. Similarly, you have an agreement in
19	place with polyARNA?
20	A Correct. And everything is open to you;
21	there's nothing to hide.
22	Q And that's a consulting agreement?
23	A It's consulting and co-founder, yes;
24	shares, things like that.
25	Q You have a copy of that?

1	A I on my computer, I doubt it. But
2	Shelly does. She has everything because she keeps
3	me compliant with the institute.
4	Q Okay. Thank you.
5	Do you have any direct consulting
6	relationship with Glaxo as an individual? Do you
7	have an individual I'll restate the question.
8	Dr. Baran, do you have an individual
9	consulting relationship with Glaxo?
10	A No, I do not.
11	Q Your interaction, professional
12	relationship with Glaxo is solely through your role
13	at Elsie?
14	A Well, it depends how you professional,
15	yeah. I have students who work there, a few
16	students who are employed there. And Glaxo will
17	reach out to me on occasion because they would like
18	to hire students, and they say, hey, Phil, we have a
19	position open, do you have any students, that kind
20	of thing.
21	But currently, no collaboration agreement
22	no consulting agreement. And I've given talks at
23	GSK over the years and been compensated for those,
24	giving those talks where you fly out and give a
25	lecture and then you go home kind of thing. But no,

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1	not like BMS, no consultant.
2	Q In terms of Nutcracker, you're on the
3	scientific advisory board, right?
4	A Correct.
5	Q And do you have an agreement with
6	Nutcracker?
7	A I do, yes.
8	Q And what is the okay. Do you have a
9	copy of that?
10	A Shelly does. You can get whatever you
11	want. It's a consulting agreement.
12	Q What is your compensation from Nutcracker?
13	A Just I believe it's just equity. I
14	didn't ask for any pay. Just some shares.
15	Q How many shares do you have?
16	A I think it's like 50,000, I think.
17	Q Do you have an idea of ballpark what
18	percentage ownership that is?
19	A It's a very minute, I don't know, sub
20	sub 1 001. It's very small.
21	Q In terms of your relationship with Elsie,
22	do you receive compensation as a consultant from
23	Elsie?
24	A No. Not one dollar.
25	Q So your financial relationship with Elsie

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1	is what is that
2	A Just equity.
3	Q Okay. What about with polyARNA?
4	A With polyARNA is equity and consulting
5	agreement for a hundred thousand a year.
6	Q Okay. And you serve on the advisory board
7	of Hongene, correct?
8	A As of a couple of months ago, yes.
9	Q Okay. What was the when did that
10	discussion start relating to your service on the
11	advisory board of Hongene?
12	A It was some time last year. David, I
13	forget his last name, contacted me and wanted to see
14	if because they're interested in getting into the
15	P(V) area and knew that, you know, our lab is doing
16	a lot of oligonucleotide work and wanted my advice
17	on, you know, high-level matters like, you know,
18	things they should sell, that kind of thing. So
19	they wanted to see if I might be interested in
20	joining the SAB. So I said okay, sure.
21	Q And what is David's last name?
22	A Is it okay for me to search my email real
23	quick to find it, or I can't touch my computer?
24	Q Sure.
25	A I can.

David Butler, B-u-t-l-e-r. 1 2 Ο So David Butler reached out to you last 3 year? 4 А Correct. 5 \bigcirc And do you know when that first date of 6 contact was? 7 Α I'm searching. Searching for the first 8 date. It was around -- looks like around July is 9 when it started, July. 10 0 July 2023? 11 July of last year, 2023, yes. Α 12 And you're looking at emails right now Q that you have that relate to --13 14 А Uh-huh, yes. 15 Who initiated the contact for your service 0 16 on the advisory board? Was it David? 17 David, he's the chief technology officer. Α 18 And is there anyone else that you -- tell Q 19 me about the process of that appointment. 20 Did you speak with anyone else besides 21 David Butler, anyone else at Hongene besides David 22 Butler? 23 Α No. He was the lead and he just contacted me and said, hey, you know, we're putting together a 24 25 newly-formed SAB, there's a couple other people in

1	
1	there, and, you know, said would you like to join.
2	That's it.
3	Q What's your compensation?
4	A I believe it is 70K per year.
5	Q And did you sign an agreement with Hongene
6	relating to
7	A I did, yes.
8	Q And you have a copy of that?
9	A Shelly does and you can have it.
10	Q Have you ever met Hongene's CEO, Dr. Wei
11	Jiang?
12	A He was at the first SAB meeting. I wasn't
13	there in person, but he was in the room on a Zoom
14	meeting like this. So I met him over Zoom or Teams.
15	Q And when was the first Hongene SAB
16	meeting?
17	A Is it okay to open my calendar and search?
18	Q Sure.
19	A The first Hongene advisory board meeting,
20	October 16.
21	Q 2023?
22	A 10:00 a.m. Pacific, yeah.
23	Q And these meetings were that meeting
24	was conducted via Zoom?
25	A I'm seeing if it was Zoom or Teams.

1	Teams.
2	Q Do you know if the meeting was recorded?
3	A I don't think it was. Recorded, but, I
4	mean, if it was, subject to them agreeing, there was
5	nothing related to this case certainly was
6	discussed.
7	I don't even know if they know I'm
8	involved. I have no clue. It was never mentioned
9	in any correspondence. They have no clue.
10	Q When you say they had no clue, who had no
11	clue?
12	A David, Wei Jiang, no one's ever mentioned
13	like, oh, I know you're involved in a case. So I
14	never said anything. And when I got invited to this
15	thing, I believe I contacted Jeremy and I said I was
16	invited to this, is it okay to do it, I don't want
17	to cause any trouble. And he's, like, there's no
18	overlap, you can do whatever you want.
19	Q And when you mean "no overlap," that means
20	what?
21	A There's no relationship of this SAB
22	meeting and the services I provide on the SAB to
23	providing expert opinions to the content of this
24	case.
25	Q When was your next did you have another

1	meeting after the October meeting
2	A That is scheduled for I don't know that
3	they have let me look at the calendar here. I
4	have a hold Shelly put a hold on my calendar for
5	February 13th, but it's a hold, which means I don't
6	know if it's the final date or not. I don't have
7	any it just says hold. So I think Shelly is
8	trying to figure out a date.
9	Q So how many meeting SAB meetings have
10	you attended?
11	A Just one.
12	Q And what did you talk about at the SAB
13	meeting?
14	A It was first David gave a really nice
15	introduction to the history of the company; all the
16	different sites, like where their revenue comes
17	from, what kind of products they work on, what areas
18	they would like to get into in the future.
19	And then, you know, they had some specific
20	questions on like trends in manufacturing, you know,
21	what areas should that are emerging should they
22	consider getting into. Like high-level discussions
23	like that, like an introductory, you know, meeting
24	to meet and greet the other the other people are
25	really well known in the field. So for all of us to

1	chat, talk, and, you know, try to provide guidance
2	to them on, you know, things that are interesting in
3	the future that the company should be looking at.
4	Q And who else was in attendance at this
5	meeting?
6	A Okay. If it's okay, I'm going to go back
7	to my calendar because I've got it all there.
8	October. Okay. So Masad Damha, he's a
9	professor.
10	Q Can you spell that for the record?
11	A At McGill. M-a-s-a-d is his first name,
12	and D as in David a-m-h-a is his last name. That's
13	he's another SAB member.
14	And then the third member is John
15	Maraganore. John is his first name and the last
16	name is spelled M-a-r-a-g-a-n-o-r-e. And then it
17	looks like Wei Jiang is there from Hongene. And
18	David Butler.
19	Q Had you met any of the other members
20	serving on the advisory board prior to this meeting?
21	A Yeah, I knew John from his time at
22	Alnylam. He's like a legend in the field of
23	oligonucleotides. And I knew Masad from oligo
24	conferences, I had met him before.
25	Q Have you ever had any relationship with

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1	Alnylam? A consulting relationship, for example?
2	A No.
3	Q At this meeting was ChemGene discussed at
4	all, ChemGenes?
5	A No.
6	Q And you testified earlier that Hongene has
7	an interest in getting involved in P(V) reagent
8	technology; is that right?
9	A Yes.
10	Q Did you talk about P(V) technology at this
11	SAB meeting?
12	A Yeah, there was a slide on it where we
13	talked about like what what are the problems,
14	what are the opportunities, what needs to be done
15	next, how does Hongene get further involved in that
16	area. There was a brief discussion on it.
17	Q And when you say "slide," is that a
18	presentation that you created?
19	A No, I didn't I didn't present. It was
20	them.
21	Q "Them" meaning Hongene?
22	A Yeah.
23	Q And were there any meeting minutes from
24	this follow-up, meeting minutes sent around to those
25	that participated?

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1	A I don't remember if there were meeting
2	minutes. But I think, look here let's see.
3	Oh, yeah, there are I have it here.
4	Let's see, what does it say? Yeah, there's a
5	document here with bullet points, meeting minutes by
6	topic. I don't know if I should read these meeting
7	minutes without you getting like, I mean, this is
8	up to Jeremy. It's kind of like, you know, it feels
9	a little slimy to tell you what they were talking
10	about.
11	But it's, generally speaking, things like
12	protein engineering, manufacturing, geopolitics,
13	de-risking, marketing, ligation technology, that
14	kind of thing. The actual details of the minutes, I
15	have to defer to Jeremy and Hongene folks and see if
16	they're willing to reveal it to you.
17	But there's nothing there. I mean, I
18	don't see anything super like, whoa, ChemGenes is
19	going to have a competitive advantage if they see
20	that.
21	Q Do you own shares in Hongene?
22	A No. I don't even know how to own shares
23	in Hongene.
24	Q Did they offer you that as part of your
25	compensation, shares in their company?

1	A No.
2	Q So the only compensation that you receive
3	from Hongene is \$70,000 per year?
4	A Correct.
5	Q And are there meetings scheduled for this
6	year?
7	A Yeah, like I said, there's a hold on my
8	calendar for February 13. But it's a hold, so I
9	don't know if that's a final date or not. That's
10	Shelly usually just puts hold on the calendar when
11	there's a tentative time, but it hasn't been
12	confirmed, so I don't know if that's a confirmed
13	date.
14	Q Is there any agreement between you and
15	Hongene relating to IP that you might develop while
16	you serve on the advisory board?
17	A No. I mean, there may be something in the
18	contract that's, like I don't think so because it
19	has to be attached to that is the Scripps uniform
20	consulting agreement, which doesn't let me
21	wouldn't let me do that. So, no, I don't think
22	that's allowed.
23	Q And Shelly has a copy
24	A Shelly has a copy, yup. You're going to
25	get like a hundred documents from her after this.

1	
1	Q And did you know David Butler prior to
2	prior to 2022?
3	A Prior to no, I didn't know him prior to
4	2023 when he contacted me in whatever it was, May,
5	July, I don't remember the first contact. But no, I
6	didn't know anybody at Hongene personally.
7	Q So you didn't know the CEO, Dr. Wei Jiang,
8	prior to 2022?
9	A No.
10	Q You're familiar with the District Court
11	case that was filed by ChemGenes against Hongene in
12	2022?
13	A If is it in one of my have I opined
14	on it in one of my declarations?
15	Q You're saying just sitting here you don't
16	remember?
17	A No, I don't know anything about that. Or
18	maybe maybe Jeremy sent something to me, but I
19	have no I don't know anything about that.
20	Q Okay. When were you first contacted by
21	who first contacted you with respect to the
22	litigation involving Hongene and ChemGenes, who from
23	who contacted you about that?
24	A I believe it was Jeremy on the line here.
25	Q And was that

1	A He would have the accurate date. He would
2	have the date unless you wanted me to search
3	through emails, but he probably has it on his
4	notepad.
5	Q And was that in connection with these
6	IPRs, or was that in connection with the District
7	Court action?
8	A He would know exactly what there's a
9	lot of stuff going on here. But it's the '885,
10	there's the two patents that we were that this is
11	supposed to be about today.
12	So Jeremy would that's a legal
13	question, you should ask him exactly what he
14	contacted me for. I get them all mixed up.
15	MR. SHORES: All right. Can we go to
16	Exhibit 2042.
17	(Exhibit 2042 marked for identification.)
18	Q Do you see this document, Dr. Baran?
19	A Yes.
20	Q Have you seen this before?
21	A Maybe. It doesn't look familiar. I
22	looked at a lot of documents, so I don't know if
23	this is one I've seen.
24	Q You just don't remember?
25	A I don't remember, no.

1	Q This is you know, for the record, this
1 2	is the Second Amended Complaint filed by ChemGenes
3	against Hongene in the District of Massachusetts,
4	which was originally filed in February of 2022.
5	And really my question is were you
6	retained as an expert in connection with this
7	District Court litigation, or were you retained
8	solely in connection with the IPRs which are
9	separate proceedings in the U.S. Patent and
10	Trademark Office which we're, you know, currently
11	litigating?
12	A Certainly you know the answer to the
13	question and I know Jeremy does, so maybe we should
14	just ask him. I don't remember.
15	Q That's fine.
16	MR. SHORES: Okay. Thank you. You can
17	take the exhibit down.
18	Okay. Maybe take a break?
19	THE WITNESS: Sure.
20	(Recess 11:29 a.m 11:36 a.m.)
21	BY MR. SHORES:
22	Q Dr. Baran, we talked earlier about your
23	affiliation with several companies and your
24	financial relationship with those companies.
25	Do you recall?

1 А Yes, sir. 2 Ο I just had a few questions, follow-up 3 questions. 4 With respect to your arrangement with 5 Elsie, you testified that you have stock ownership 6 in Elsie, correct? 7 А Correct. 8 Do you have stock options as well? 0 I think -- options. I don't know if 9 А 10 they're options or just granted shares. 11 But that would be reflected in your 0 12 agreement with Elsie? 13 А Nothing is secret. You can have it all. 14 Q And then with respect to your arrangement 15 with polyARNA, does that arrangement include stock 16 options? 17 You'll have to look at the contract. Α Τ think I just, again, have shares. I don't know if 18 it's listed as an option or as a share, but when you 19 20 get the document, you'll see it. 21 Similarly, with respect to Nutcracker Q 22 Therapeutics, do you have stock options in 23 Nutcracker Therapeutics? 24 I think they are options, but they may А vest at a certain point. I think -- I recall 25

1	because I have that Carta app and it shows what you
2	have I think they are referred to as options and
3	they vest over time, I think.
4	Q Okay. And what about your arrangement
5	with Hongene, do you have any stock options with
6	Hongene?
7	A No.
8	MR. SHORES: Okay. If we could put up
9	Exhibit 1004.
10	(Exhibit 1004 marked for identification.)
11	Q Do you see this document, Dr. Baran?
12	A Yes, I do.
13	Q And you're familiar with this?
14	A Yeah. This is the Aerschot J. Med. Chem
15	document.
16	Q And this this exhibit, you referenced
17	this exhibit in connection with the your your
18	declaration relating to the '569 patent, correct?
19	A Correct, yes.
20	Q And you cited this reference as an
21	anticipatory reference to claims 1 and 2 of the '569
22	patent?
23	A Correct.
24	Q How did you find this this article?
25	A It was either either I think I found it

1	or the coursel found it. We collaborated to find
1	or the counsel found it. We collaborated to find
2	it. And I was informed basically of the species
3	genus legal principle that, you know, anticipation
4	of a single species in a claim genus anticipates the
5	entirety of the genus. And so as a matter of
6	efficiency, we just identified this one to
7	anticipate claims 1 and 2 of the '569 patent.
8	Q Were you aware of this publication before
9	you began consulting on the case?
10	A I mean, I'm not sure. I've read thousands
11	and thousands of papers over the course of my
12	career, so I don't remember.
13	Q Okay. Could you read the first line of
14	the abstract into the record, please?
15	A Sure. Let me zoom in a little bit.
16	Q Starts with "A series."
17	A Yeah, let me zoom in.
18	"A series of 2 prime- and 3 prime-
19	fluorinated 2 prime, 3 prime-dideoxynucleosides and
20	3 prime-azido-2 prime, 3 prime-dideoxynucleosides
21	were synthesized and evaluated for their inhibitory
22	activity against human immunodeficiency virus-1
23	(HIV-1) replication in MT-4 cells. Neither
24	conversion of 3 prime-fluoro or 3 prime-azido-2
25	prime, 3 prime-dideoxyadenosine to the corresponding

1	incaine derivatives nor 0 bromination of 2 prime 2
	inosine derivatives nor 8-bromination of 2 prime, 3
2	prime-dideoxyadenosine resulted in increased
3	anti-HIV-1 activity, nor did"
4	Q Sorry to interrupt. I just don't want
5	to I was just asking for the first sentence and I
6	just didn't want you to have to read the entire
7	abstract
8	A Oh, okay.
9	Q that first sentence, so.
10	A Sure, whatever.
11	Q And then in the first paragraph, it
12	states, "The discovery of the human immunodeficiency
13	virus (HIV) as a causative agent of AIDS 1,2 and the
14	identification of HIV as a retrovirus have prompted
15	the search for agents that would be able to block
16	the HIV replication process."
17	Did I read that correctly?
18	A Yes.
19	Q And after it reads, "Our efforts have
20	mainly focused on the design and synthesis of
21	reverse transcriptase inhibitors. 2 prime, 3
22	prime-dideoxynucleoside analogues" and later,
23	"have attracted considerable attention as an
24	anti-HIV compound, and several congeners of this
25	class are currently subject to clinical trials."

1	Did I read that correctly?
2	A Yes.
3	Q So is it fair to say that this publication
4	concerns the development of the anti-HIV compound?
5	A Yeah.
6	Q Okay. And is it fair to say there's
7	nothing in Aerschot that talks about the synthesis
8	or use of any phosphoramidite?
9	A That is correct.
10	Q And is it fair to say that there's nothing
11	in Aerschot that talks about the synthesis or use of
12	any oligonucleotide?
13	A I don't see any oligonucleotides in here.
14	Q And Aerschot, this reference does not
15	report on oligonucleotides synthesis in the
16	conventional 3 prime to 5 prime direction, correct?
17	A Correct.
18	Q And Aerschot does not this reference in
19	Aerschot does not report on oligonucleotide
20	synthesis in the unconventional 5 prime to 3 prime
21	direction, right?
22	A Correct.
23	MR. SHORES: Okay. If you can go to if
24	we can pull up Exhibit 1003 from the '569
25	proceeding.

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1	
1	Q Okay. If we can go to paragraph 20.
2	A Give me a second.
3	Q Yeah, no problem.
4	A 20. Okay. I'm there.
5	Q In paragraph 20, you testified that "Both
6	the '569 patent and the relevant prior art relate to
7	reverse RNA oligonucleotide synthesis using reverse
8	phosphoramidite chemistry."
9	Did I read that correctly?
10	A Yes.
11	Q That's your testimony?
12	A Yes.
13	Q And by "relevant prior art," you're not
14	referring to Aerschot; correct?
15	A That prior art doesn't refer, obviously,
16	to reverse RNA oligonucleotide synthesis.
17	Q Right. So your testimony and the
18	testimony just read into the record, you're not
19	by "relevant prior art" you're not referring to
20	Aerschot?
21	A Aerschot only invalidates claims 1 and 2
22	because they're anticipated, that's all.
23	Q So just again, my question is by "relevant
24	prior art" here you're not referring to Aerschot,
25	correct?

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1	A The only relevancy of Aerschot is to
2	render claims 1 and 2 invalid.
3	Q Respectfully, that's not answering my
4	question.
5	My question was by "relevant prior art"
6	here you're not referring to Aerschot, correct?
7	A I think you asked it and I answered it
8	already. Aerschot does not refer to reverse RNA
9	oligonucleotides synthesis, again.
10	Q So the answer is no?
11	MR. EDWARDS: Object to form.
12	Q I'm just looking for an it's a simple
13	yes or no question.
14	A I'm just giving you
15	MR. EDWARDS: There's no question.
16	(Court Reporter clarification.)
17	Q Yeah, understood.
18	I'm just I keep asking it. I think
19	it's a pretty pretty clear yes or no.
20	Here in paragraph 20 of your declaration
21	in Exhibit 1003, by "relevant prior art" you are not
22	referring to the Aerschot reference, correct?
23	MR. EDWARDS: Form. Asked and answered.
24	MR. SHORES: Hasn't been answered.
25	A All I can say is that the relevance of

1	Aerschot is only with regards to the anticipation of
2	claims 1 and 2 rendering them emphatically and
3	unassailably invalid.
4	Now, with regards to Aerschot's
5	participation in RNA oligonucleotide synthesis, it
6	has nothing to do with that.
7	Q Aerschot has nothing to do with reverse
8	RNA oligonucleotide synthesis, correct?
9	A That paper is not about that at all. But
10	the building block described therein is useful for
11	potentially useful for the purposes of RNA or
12	reverse RNA synthesis.
13	Q Isn't it correct that Aerschot doesn't
14	teach a POSA anything about oligonucleotide
15	synthesis?
16	A Well, that's not true, because a POSA who
17	needs to make an oligonucleotide would look for
18	monomers, and they would look for preparation of
19	monomers, and they would find in Aerschot a very
20	good and reliable preparation of a monomer that
21	could be used in oligonucleotide chemistry.
22	Q But Aerschot doesn't relate to
23	oligonucleotide synthesis, though.
24	A It doesn't need to.
25	Q Does it or doesn't it?

1	You've already testified to this, so I'm
2	just
3	A Well, Aerschot reports a tool and that
4	tool is a compound and that compound can be used for
5	HIV, but it can be used for other things as well.
6	So a POSA would use that reference in
7	order to make analogs containing that nucleoside.
8	They wouldn't look at that reference and say, oh,
9	those building blocks that are super useful for my
10	study, I can't use them because HIV is in the title.
11	Does that make sense?
12	Q I'll take it as a non-answer.
13	A Okay.
14	Q What's the what is the advantage of
15	5 going, you know, in the reverse direction
16	synthesizing oligo going from 5 prime to 3 prime,
17	why are there any advantages that's conferred by
18	that process versus the 3 prime to 5 prime
19	synthesis?
20	A Well, as is known in that field of, you
21	know, reverse oligonucleotide synthesis, on occasion
22	it can have benefits in terms of purification
23	efficiency, coupling coupling efficiency. There
24	are times when one would want to employ that.
25	Q And are there any specific applications

1	that you can identify where 5 prime to 3 prime would
2	be a more useful tool than 3 prime to 5 prime when
3	synthesizing an oligo?
4	A I mean, it's case dependent. The vast
5	majority of folks will do it in the canonical
6	fashion. And if they encounter problems, they may
7	then start looking at the reverse method that, you
8	know, I think I referenced some papers in my
9	declaration, some (indiscernible) paper. There's a
10	few papers in this area that talk about reverse
11	oligonucleotide synthesis and how it can be
12	advantageous on some occasions. It's not often
13	used.
14	Q "It" being the 5 prime to 3 prime?
15	A The reverse method.
16	Q And do you use this in any of your work,
17	the process of 5 prime to 3 prime synthesis?
18	A No.
19	Q Has anyone on any of your teams used
20	this
21	A They may have.
22	Q to your knowledge?
23	A It's possible, but I just don't know.
24	It's possible. I see tons and tons of experiments,
25	so I don't remember.

MR. SHORES: Okay. If we can go to 1 2 Exhibit 1011, please. 3 (Exhibit 1011 ('707) marked for 4 identification.) 5 Have you seen this document in Exhibit Ο 6 1011, Dr. Baran? 7 Α Yeah, I believe I reference this in my 8 declaration. 9 Okay. It's a publication from 2000 by 0 10 Wagner; is that right? 11 Mm-hmm, yes. Α 12 Q And it's titled "Synthesis of 13 2'-Deoxyribonucleoside 5'-Phosphoramidites: New Building Blocks for the Inverse (5' to 3')-14 15 Oligonucleotide Approach." 16 Did I read that correctly? 17 А Yes. 18 And then you cited to this in connection Q with your declaration that supported the petition 19 for the '707 patent, correct? 20 А 21 Yes. 22 And so you read this article before you Q 23 signed your declaration, correct? 24 Α Yeah. 25 Thank you. Q

1	And how did you find this article?
2	A Just literature searching.
3	Q Okay. So you found this article?
4	A I believe I found it. But, you know, we
5	pass between the counsel and I pass a lot of
6	papers between each other, but I believe this is one
7	of the ones that I independently found as well.
8	They may have found it, too.
9	Q Were you aware of this publication before
10	consulting on this case?
11	A Maybe. I don't remember. As I said, I've
12	read thousands of papers over the years.
13	Q And then looking on the first page, do you
14	see there's a it's the second sentence in the
15	first introduction paragraph starts with "Even
16	though"?
17	A Yes.
18	Q Okay. It says "Even though" I'm going
19	to read it into the record.
20	"Even though primary phosphoramidites are
21	often used for the synthesis of 3 prime to 3 prime
22	and 5 prime to 5 prime internucleotide linkages,
23	very little is known in literature about the
24	detailed specification of the synthesis of the
25	appropriate 5 prime phosphoramidites suitable for

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1	the built up of eligenucleatides in the 5 prime to 2
1	the built-up of oligonucleotides in the 5 prime to 3
2	prime direction."
3	Do you see that?
4	A Yes.
5	Q Do you agree with that statement?
6	A I mean, it's a peer-reviewed paper, and at
7	the time of the publication we have to assume that
8	that's a correct assessment.
9	Q So is it fair to say that based on this
10	statement, that 5 prime to 3 prime direction
11	synthesis was still in its infancy when this article
12	came out?
13	A I don't know if "infancy" is the right
14	word. But in 2000 that's the statement they write
15	that passed peer review.
16	Q And it's fair to say at the time this
17	article was released, there was much research to be
18	done to understand how to run oligo synthesis in the
19	reverse direction?
20	A That might be true, but I really haven't,
21	as part of this declaration, been asked to, you
22	know, research this super heavily. The substance of
23	my declaration is just in anticipation of claims 1
24	and 2 as they are anticipated.
25	Q Would you is it fair to say that
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1	traditional synthesis, you know, 3 prime to 5 prime,
2	was more common in the early 2000s?
3	A It's probably true. But I would need to
4	do a, you know, moreto come up with a guaranteed
5	answer more more searching and reading to make
6	sure that that was a correct assessment. But it's
7	not what I was asked to opine on for these
8	declarations.
9	Q What about sitting here, sitting here
10	today, is the traditional 3 prime to 5 prime is
11	more common than 5 prime to 3 prime, right?
12	A As of today, it's still more common for
13	people to employ the 3 prime to 5 prime.
14	Q Right. So back in 2000, the 5 prime to 3
15	prime wasn't really an established technique?
16	A I mean, it's established in this paper.
17	And, you know, as I said already, that I would need
18	to do much more reading and analysis because that's
19	not what I was asked to opine on.
20	Q And if you look at the bottom of the
21	introduction, still on this page here, it starts
22	with "Application."
23	Do you see that?
24	A Yes.
25	Q Could you read that sentence into the

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1	totally unprotected oligonucleotides?
2	A Due to the totally unprotected
3	oligonucleotides? No. It's the use of that
4	strategy that that allows for yeah, without
5	having to protect, I believe, it's the nucleobase.
6	But let me see here. No, it is on the nucleobase
7	that they are protected.
8	Q Right. So sorry. Go ahead.
9	A No, go ahead.
10	Q Okay. So it's the protecting groups
11	are being used that that's what causes the high
12	purity, but it's not really the synthesis, the
13	synthesis process itself, right?
14	A I don't think you can make that inference.
15	It's a culmination of both features that you're
16	going in a reverse direction and they find using
17	these protecting groups as advantageous for that.
18	Q So where in this reference does it
19	indicate that the reverse synthesis has a you
20	know, causes the higher purity in the
21	oligonucleotide?
22	A If you give me a few minutes, I'll scan
23	through.
24	Q Okay.
25	A Well, one of the advantages that's clear

1	is if you want to conjugate something to the 3 prime
2	end, that's going to be impossible to do with the
3	conventional approach because it's connected to a
4	resin.
5	So with regards to making specific
6	modified oligo sequences that have, for instance,
7	something unusual at the end, the conventional
8	strategy won't let you do that. And that's
9	exemplified in the end here. It's just one example,
10	but I'd have to read more on this.
11	Q So it's your testimony is definitely the
12	protecting groups have something to do with it, but
13	you're also saying that the the direction also
14	has something to do with it as well, "it" being the
15	achievement of higher purity in the oligonucleotide?
16	A I didn't say higher purity. But in terms
17	of actually making, you know, conjugates where
18	something is terminating on the 3 prime division,
19	you can't easily do that with the conventional way
20	of making oligos because it's connected to the
21	resin. So once you de-protect it, it's over.
22	Q But I guess I'm trying to clarify. I want
23	to understand here.
24	So the protecting groups have this
25	paper is about the protecting groups having an

1	effect a positive effect on purity, correct?
2	A Among other things. But the reverse
3	oligonucleotide synthesis in this paper is allowing
4	them to make constructs that would be difficult to
5	make with the conventional means of oligo synthesis.
6	Q So your testimony is you would need both
7	the protecting groups, but also the reverse
8	synthesis?
9	A No, that's not my testimony. I mean, as I
10	said, this is not a topic I was instructed to study
11	in great detail. I'm looking at the paper now. I
12	read it, but it's not what is in my declaration.
13	My declaration is mainly concerned with
14	as a background matter for the folks involved, the
15	history of oligonucleotide synthesis to put things
16	in perspective. But as a factual matter, the
17	anticipation of claims 1 and 2, that's the main
18	heart of the declaration in both cases.
19	MR. SHORES: If you can put up Exhibit
20	1012 from the '707 IPR.
21	(Exhibit 1012 ('707 IPR) marked for
22	identification.)
23	Q And have you seen this document,
24	Dr. Baran?
25	A I think so.

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1 Okay. What's your -- what is this Q 2 document? 3 This is a publication on making various Α 4 microarrays using synthesis in the reverse 5 direction, making those microarrays using the 6 reverse direction modality. 7 And it's titled "Light-directed 5 prime to Ο 8 3 prime synthesis of complex oligonucleotide microarrays." Is that correct? 9 10 А Yes. And you cited to this in your declaration 11 0 12 that you submitted in connection with the '707 patent; is that right? 13 14 А Mm-hmm, yes. And you reviewed this publication? 15 0 16 I read it, yes. Α 17 You agree with its contents? 0 18 I mean, I agree that this is a published Α 19 But I don't know if I agree with every paper. 20 single word that's written. I didn't write the 21 paper. 22 The paper relates to the synthesis of DNA Q in the 5 prime to 3 prime direction, correct? 23 24 Mm-hmm, yes. Α 25 It doesn't report any results for RNA Q

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1	synthesis, correct?
2	A I have to check. I don't think so.
3	That's not what the what the point of this was
4	was for DNA. It doesn't say RNA.
5	Q Okay. If you want to take a look to
6	confirm, that's fine.
7	A Looks like only DNA here.
8	Q Okay. And so it doesn't have synthesis of
9	RNA in the 5 prime to 3 prime direction, correct?
10	A Not in this paper, no.
11	Q The focus is on DNA in this publication,
12	right?
13	A Looks like it, yes.
14	Q So if you look at the sentence on the
15	bottom of page 4, the bottom left, starts with "This
16	is consistent"
17	A Page 4?
18	Q Yes, on the bottom left. You can see the
19	it's like six lines up from the bottom. It says,
20	"This is consistent with"
21	A Yeah.
22	Q So that sentence says, "This is consistent
23	with previous studies using DMT based 5 prime to 3
24	prime synthesis. Stepwise yields are slightly lower
25	on average than 3 prime to 5 prime synthesis using

1	NPPOC chemistry, even with longer coupling times."
2	Did I read that correctly?
3	A Yes.
4	Q Is it fair to say that the authors here
5	found oligonucleotide synthesis in the 5 prime to 3
6	prime direction vis-a-vis synthesis in the 3 prime
7	to 5 prime resulted in poor coupling yields?
8	A I mean, that's what they say. But it's a
9	very different strategy. They are doing this on
10	arrays, which could be different than an
11	oligonucleotide synthesizer.
12	And if your purpose was to have a
13	construct with something connected at the 3 prime
14	position, C 3 prime position at the end, your best
15	bet would be to do reverse if you wanted to change
16	the nature of the group at the end point.
17	So 5 prime to 3 prime could have
18	advantages with regards to purity, depending on the
19	building blocks you used and depending on the kind
20	of construct you're trying to make.
21	But for further, you know, in-depth study
22	and evaluation and analysis, that would be something
23	I would need to spend a lot of time and and
24	specifically be asked to opine on, and that's not
25	what I was asked to do.

1	Q So if you look at Table 1 on page 2, is it
2	fair to say that this shows a higher stepwise yield
3	for a 3 prime to 5 prime than 3 (audio disruption).
4	(Court Reporter clarification.)
5	Q Versus 5 prime to 3 prime with every base?
6	A I mean, it really depends on if the if,
7	you know, how many data points there are, if this is
8	a really rigorous statistical analysis.
9	The yields are close, they are very close,
10	number one. Number two, they are done on a
11	microarray, which is a very specialized type of
12	oligonucleotide synthesis.
13	Q Is it fair to say that the poorer coupling
14	yields shown here would render synthesis of longer
15	oligonucleotides less plausible?
16	A No, I don't know that you could say that
17	based on what is seen here, because I don't know how
18	much time has gone in to optimize. And again, this
19	was done on an array, not on an oligo synthesizer.
20	So there could be different variables to explore.
21	Q But this paper doesn't teach synthesizing
22	oligonucleotides in the 5 prime to 3 prime would
23	necessarily produce longer oligos than synthesis of
24	3 prime to 5 prime, right?
25	A Yeah, I would have to study it more. I

1	don't know if it teaches that or not. I would need
2	time to look at this and look at the context.
3	Again, this was not a topic I was asked to study in
4	depth.
5	Q So sitting here today, you can't point to
6	anything that indicates that the synthesis of oligos
7	in the 5 prime to 3 prime direction would produce
8	longer oligos than synthesis in of oligos in the
9	3 prime to 5 prime direction, right?
10	A I mean, maybe given more time and looking
11	at background literature, perhaps. But I really
12	need the time to do the proper analysis, and that's
13	not what I was asked to do.
14	Q So the answer is no, sitting here today?
15	A The answer is I don't know. I need more
16	time.
17	Q Is the answer yes, sitting here today?
18	A I think I just gave my answer.
19	MR. EDWARDS: Objection to form.
20	MR. SHORES: Okay. Can we pull up Exhibit
21	1014 from the '707.
22	(Exhibit 1014 ('707 IPR) marked for
23	identification.)
24	Q Dr. Baran, do you see this document on the
25	screen?

1	A Yes.			
2	Q Are you	familiar with this document?		
3	A Yes, thi	s is the anticipatory reference		
4	for for the other patent.			
5	Q So this	is U.S. Patent		
6	A '707.			
7	Q So this	is U.S. Patent Number 5,869,696,		
8	correct?			
9	A Correct.			
10	Q And it's	s titled "Universal Solid Supports		
11	And Methods For Th	And Methods For Their Use"?		
12	A Yes.			
13	Q And ther	this is cited in your declaration		
14	in connection with the '707 IPR, correct?			
15	A Yes.			
16	Q And you	cited it as an anticipatory		
17	reference for clai	reference for claims 1 and 2 of the '707 patent,		
18	correct?	correct?		
19	A Correct.	Correct.		
20	Q And you	ve reviewed this patent?		
21	A Yes.			
22	Q And did	you find this patent yourself?		
23	A Again, I	don't remember if it was me or		
24	counsel. We passe	ed a lot of documents back and		
25	forth to each othe	er.		

1	Q The title says "Universal Solid Support."
2	So is it your understanding that the
3	universal supports are solid supports that allow a
4	practitioner to use one type of support for an
5	oligonucleotide synthesis?
6	A "Universal" is a strong term to use. But
7	that's you know, the inclination is to inform the
8	public that this can be used for a variety of
9	different purposes.
10	Q And is it your understanding that the
11	teachings of this reference indicate that the use of
12	the disclosed universal solid support allows a
13	practitioner to avoid stockpiling different solid
14	supports?
15	A By universal, the goal would be, you know,
16	to allow people to focus on using one for all their
17	needs versus having, you know, multiple different
18	types, so yeah.
19	Q If you go to, you know, if you turn to
20	go to column 1, line 34.
21	Do you see the statement, it says,
22	"Maintaining a supply of at least 8 different
23	prederivatized solid supports is inconvenient and
24	expensive"?
25	Do you see that?

1	A Yes.
2	Q Would you agree with that statement as a
3	general proposition?
4	A I mean, it depends on the you know,
5	certainly if you had one support, it's better than
6	having eight. But if your purpose is if you're a
7	large or even a regular biotech company, you need to
8	make something, you're going to use the support
9	which is fit for purpose.
10	So yeah, I agree with the statement that
11	if you have one support that works as well as eight,
12	it's probably better to just have one.
13	Q And you agree that in solid phase
14	oligonucleotide synthesis in the traditional 3 prime
15	to 5 prime direction typically requires the use of
16	solid supports that have the 3 prime most nucleotide
17	attached to it?
18	A Yeah, that's how it works.
19	Q And if you can go to claim the claims
20	of the '696 patent, and column 33.
21	A Okay. Column 33. There's 32. 33. Okay.
22	There you go.
23	Q Okay.
24	A It went up again. Sorry.
25	Q The sequences get in the way sometimes.

1	A Yeah.
2	Q So claim 1 is directed to a cleaving
3	reagent, correct?
4	A That's what it looks like, yes.
5	Q Looks like all these claims are directed
6	to a cleaving reagent, is that fair to say?
7	A Looks like it, mm-hmm, yeah.
8	
9	are useful for moving oligonucleotides from the
10	solid support on which they are synthesized?
11	A Yeah.
12	Q And is it also fair to say that these
13	claims are not directed to oligonucleotide
14	synthesis?
15	A I think they well, I mean, there are
16	oligonucleotide cleaving reagents, though, by
17	definition, they are useful for the synthesis of
18	oligonucleotides.
19	Q Do they do these claims indicate
20	synthesis in either the 5 prime to 3 prime or the 3
21	prime to 5 prime direction?
22	A I don't know that that's relevant here.
23	Q I'm just asking you
24	A I don't know. I would have to, you know,
25	refresh my memory on the go through the written

description. But either way, the claims are to 1 2 cleaving reagents, so... Right. Okay. So they are to cleaving 3 Q 4 reagents. 5 I'm just talking about the claims, not the 6 description. I'm asking -- the claims aren't 7 directed to 5 prime to 3 prime or 3 prime to 5 prime 8 synthesis, right? They could -- the claims don't have that 9 А 10 written in them, correct. And then the claims are also not directed 11 0 12 to nucleosides, correct? 13 No, doesn't look like it. А 14 Q And they are not -- okay. Thank you. 15 And they are also not directed to 16 phosphoramidites? 17 The claims, no. А And they are not -- the claims aren't 18 Q 19 directed to solid supports either; is that right? 20 А I don't see anything regarding a solid 21 support on these claims, no. 22 Q Okay. 23 MR. SHORES: I think we're probably at a 24 good stopping point here. I think we probably want 25 to take a lunch break.

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1	Deep that work for arough dw2. Dr. Denor
1	Does that work for everybody? Dr. Baran,
2	you're on a different timetable, so I don't know if
3	you
4	THE WITNESS: Lunch would be great. I've
5	been waiting all day. I'm happy to go as long as
6	you want. You're the boss, you tell me what to do.
7	MR. SHORES: Maybe we can maybe we can
8	take, you know, about maybe 45 minutes.
9	THE WITNESS: Can you just give me an
10	exact time to come back to this computer and then
11	I'll be here promptly at that exact time.
12	MR. SHORES: Why don't we come back at 12
13	or our time it actually would be I guess 1:15.
14	Am I getting that right? Hold on. Yeah.
15	1:15.
16	THE WITNESS: 1:15. Okay.
17	MR. EDWARDS: 1:15 Eastern we'll be back.
18	(Recess 12:22 p.m 1:23 p.m.)
19	BY MR. SHORES:
20	Q All right. Dr. Baran, we talked before
21	the break we talked about your agreement with
22	Hongene.
23	Do you recall that testimony?
24	A Yes.
25	Q And how long does that agreement go for?

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1	How long is your contract for?
2	A I think it's like every year they can
3	renew it. I don't think it's binding for more than
4	a year. But again, I defer to the document that you
5	are free to get.
6	Q And to your knowledge, does Hongene
7	in-license any P(V) technology?
8	A Currently, no.
9	Q Is that to your knowledge, or no
10	A To my knowledge.
11	Q Okay. Is it possible they could
12	in-license it, but you don't know one way or the
13	other?
14	A Anyone could in the future, even
15	(indiscernible).
16	(Court Reporter clarification.)
17	A I said anyone could in the future,
18	ChemGenes, Glen, anyone who wants.
19	Q So would Elsie be in a position to license
20	that type of technology let me ask it again a
21	different way.
22	Would Elsie consider licensing P(V)
23	technology to Hongene?
24	A I don't think they legally can. I think
25	that needs to be done like a for selling

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1	reagents, I think they need to go work with BMS on
2	that. I don't think Elsie has the right to
3	sublicense things for reagents.
4	Q So if a company wanted to license P(V)
5	reagents, to your knowledge, they would approach
6	BMS?
7	A Correct.
8	Q And to your knowledge, MilliporeSigma is a
9	current, I guess, sublicensee of the technology?
10	A Correct.
11	Q Are there any other licensees or
12	sublicensees to the P(V) reagent technology, to your
13	knowledge?
14	A Aside from Elsie and Sigma-Aldrich, not to
15	my knowledge.
16	Q And do you have any other agreements with
17	Hongene besides the agreement that you referenced
18	earlier that relates to the service on the advisory
19	board?
20	A No.
21	Q And it's your understanding that Hongene
22	sells phosphoramidites as part of its product
23	offering?
24	A Yes.
25	Q And you've have you ever been

1	affiliated with an organization that's purchased
2	Hongene phosphoramidites?
3	A I believe all the companies I work with
4	have ordered from every vendor out there; ChemGenes,
5	Hongene, Glen, TCI, Aldrich. Organizations don't
6	really care where they buy from. If it's commercial
7	and reasonably priced, they buy it.
8	Q And you characterize, you know, ChemGenes,
9	Hongene as competitors in the marketplace?
10	A They're all selling reagents. So, yeah,
11	it's a it's a crowded market. So, you know,
12	ChemGenes, Hongene, Glen, to some extent Sigma,
13	other vendors, Combi Blocks, TCI.
14	But the vendors that specialize in, like,
15	you know, oligo-specific stuff and go to a lot of
16	conferences are places like ChemGene, Hongene, Glen,
17	and there's probably some other boutique reagent
18	suppliers that are heavy into the oligo space.
19	MR. SHORES: So if we can pull up Exhibit
20	1003 from the '569.
21	Q We looked at this exhibit earlier today.
22	Do you recall?
23	A Yes.
24	Q And this is a copy of your declaration in
25	support of petition for IPR relating to the '707

1	patent?
2	A Correct.
3	Q Okay. And if we go to paragraph 21 of
4	this document or, excuse me, paragraph 20.
5	Actually, I think the wrong exhibit is up.
6	This exhibit is okay. Well, I asked
7	for the exhibit to the '569, but that was the
8	exhibit for the '707. We can still use that
9	document. I just was looking to start with '569.
10	But this is fine.
11	So you see here in paragraph 20, you see
12	the statement?
13	A Yeah.
14	Q Okay. And do you still agree I'm
15	sorry the testimony that is provided in paragraph
16	20 says, and I'll read it into the record, "In my
17	opinion, a POSA would have had a Ph.D. (or
18	equivalent) in organic or medicinal chemistry, and
19	two to three years of postgraduate work experience
20	in medicinal chemistry, synthetic organic chemistry,
21	and nucleic acid chemistry, including the
22	development of oligonucleotide therapeutics,
23	diagnostics, or building blocks. Alternatively,
24	someone who had extensive work experience in these
25	fields, and who had gained a thorough understanding

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1	of the development of nucleic acid-based materials,
2	would also have qualified as a POSA with a
3	bachelor's or master's degree in organic chemistry
4	or medicinal chemistry."
5	Did I read that correctly?
6	A Yeah.
7	Q And you agree with that testimony?
8	A Yes.
9	Q Under this definition, if a person had all
10	the qualifications that are described here, but did
11	not have work experience in medicinal chemistry,
12	would they still qualify as a POSA?
13	A I'm not sure. You would have to look at
14	it at a case-by-case basis and see what their
15	experience was. I'm not I don't know if we
16	can you know, it has to be taken on a
17	case-by-case basis perhaps.
18	Q In connection with the claims of the '707
19	patent and the claims of the '569 patent, those
20	claims are directed to building blocks, correct?
21	A Correct.
22	Q Including phosphoramidites, correct?
23	A Including phosphoramidites and some
24	precursors thereof.
25	Q And nucleosides?

1	A Yes.
2	Q Okay. They are not those claims, the
3	claims in the '707 patent, are not directed to
4	oligonucleotides, correct?
5	A For claims 1 and 2, they are just
6	compounds, building blocks, as you said.
7	Q And they are not directed to therapeutics,
8	correct?
9	A I would have to read the claim language,
10	but I think they are just building blocks.
11	Q Same with the '569, claims 1 and 2 of the
12	'569 patent, are those claims just directed to
13	building blocks?
14	A As I recall, yes.
15	Q And those claims are not directed to
16	oligonucleotides, correct?
17	A I don't believe so. I think they are just
18	building blocks.
19	Q Those claims in the '569 patent, claims 1
20	and 2, are not directed to therapeutics, correct?
21	A If you want to show the document really
22	quick to make sure, but I don't as I recall, they
23	are just building blocks.
24	Q Is it fair to say that the building blocks
25	that are claimed in the '707 and '569 patent may not

1	have been used for therapeutic purposes?
2	A That's fair.
3	Q And from the perspective of a medicinal
4	chemist, can you describe the role that a medicinal
5	chemist plays in this in the development of a
6	therapeutic, for example?
7	A Sure. A medicinal chemist working in this
8	area might have a need for a tool compound, they may
9	have a need for a model compound that may not be a
10	therapeutic, or they may be working on something
11	which is deliberately intended to be used for
12	therapeutic purposes.
13	And in the process of doing the medicinal
14	chemistry on that, they would have a target
15	sequence. They would explore various permutations
16	of the ribose structure and fashion a route based on
17	that target sequence that would reliably work in the
18	oligonucleotide synthesizer to deliver the desired
19	product for some sort of assay or readout to check
20	for properties. That's like really high level.
21	Q Right, right. That's fine.
22	So when you're talking about a target
23	sequence, is there an example of a particular
24	disease that an oligo is used to treat or to, you
25	know, mitigate the effects of?

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1	A Well, it depends what kind of oligo. I
2	mean, there's famous examples like the COVID
3	therapeutic mRNA. And then there's if you're
4	talking about a smaller oligonucleotide, you can
5	think of another famous example, which is Spinraza,
6	which is an antisense nucleotide, so it's much, much
7	smaller. Both of those are therapeutic
8	oligonucleotides.
9	Q So you would consider the mRNA an
10	oligonucleotide, right?
11	A That's what it is.
12	Q Is it fair to say it's a rather lengthy
13	oligonucleotide?
14	A Like I said before, oligo, if you define
15	it, is two or more. So it can be several hundred
16	and it can be 15, and you still classify it as
17	oligonucleotide.
18	Q Okay. That's fair.
19	I think a lot of times the conversation
20	around some of these oligonucleotides is that they
21	are a certain limited size in mers, but an mRNA
22	molecule is larger. So I was just looking for that,
23	you know, distinction. Thank you.
24	A Sure.
25	Q Now, for the shorter oligonucleotide

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1	sequences, are those how are those I'm sorry.
2	My understanding is messenger RNA
3	therapeutics is delivered the payload, the mRNA
4	payload, like, for example, in the COVID vaccine, is
5	delivered via a lipid nanoparticle delivery system
6	that interacts with the cell and the cell takes
7	the takes the payload up into its cell and then
8	it affects the therapeutic by causing the cell to
9	produce, you know, the subject protein there, the
10	spike protein from the coronavirus.
11	Are the shorter oligos maybe "shorter"
12	isn't the right term but oligos that are, you
13	know, shorter in length, are they delivered the same
14	way? Are they delivered via lipid nanoparticle?
15	How do those therapeutics make their way
16	into the cell?
17	A Yeah, it's a good question, and it really
18	depends. So, for example, bigger oligos but not
19	quite as big as mRNA, like siRNA, are usually
20	formulated with some sort of lipid nanoparticle on
21	occasion. Often the they also have some kind of
22	conjugation to something which makes them localized
23	in an organ or behave better.
24	So, for example, some ASOs and some
25	smaller oligos are connected to sugars to, you know,

1	improve their properties. But sometimes ASOs can be
2	delivered just as, you know, the oligo by itself in
3	a formulated solution with various excipients. And
4	in the case of something like Spinraza, you've got
5	direct injection into the spinal fluid of an infant.
6	So it really depends on that goes down
7	to a formulation conjugation question, and the
8	delivery is a really hot and important topic in the
9	oligonucleotide world.
10	Q And are you are you familiar, you know,
11	whether mRNA the mRNA utilized, for example, in
12	these, you know, coronavirus vaccines, the ones that
13	are produced by Moderna and BioNTech with Pfizer,
14	are those phosphodiester backbones or do they have
15	different backbones?
16	A They feature unusual (audio distortion).
17	(Court Reporter clarification.)
18	A They feature unusual bases. So N-methyl
19	pseudouridine is a common base that you can find in
20	an mRNA vaccine to reduce immunogenic properties and
21	make it safer. But, to my knowledge, they don't
22	contain phosphorothioate.
23	Q So when a medicinal chemist is evaluating
24	a, you know, candidate, and if the candidate is an
25	ASO

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1	A Okay.
2	Q for a particular, you know, indication,
3	what does that process involve?
4	Is there an example of a medicinal chemist
5	designing an ASO and then applying that to a
6	particular a particular disease?
7	A Yeah. So Spinraza, since I mentioned it,
8	is a good sort of flagship example that a lot of
9	people like to use. That one was discovered through
10	first a bioinformatics search on an mRNA transcript
11	to find what would be an ideal, a good sequence.
12	I suppose several candidates were made,
13	various analogs were made. And then I believe it's
14	a 17 mer, I'm not I think it's a 17 mer, and then
15	it contains within it all the linkages are
16	phosphorothioate linkages.
17	Q And then the Spinraza, how what's
18	the you know, how does that how does that
19	treat the disease?
20	Does it make its way into the cell and is
21	it interfering RNA? How does it work?
22	A So it's a steric block antisense
23	oligonucleotide. And I think how it works is you
24	inject it directly into the cerebral spinal fluid,
25	it has a half life of about half a year, so the

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1	indication. Is that fair to say?
2	A Yeah, I think that's fair to say, mm-hmm.
3	Q So when the medicinal chemist is building
4	or wants to build that therapeutic, the medicinal
5	chemist will look towards will utilize building
6	blocks or cause others to utilize building blocks in
7	order to construct the subject therapeutic, right?
8	A Well, eventually what will eventually
9	become the therapeutic, yeah. So they're looking
10	for lead compounds, they might test 10, 20, a
11	hundred or more various leads and they'll run them
12	through a battery of different assays and then go to
13	a rodent perhaps and then maybe a dog. And once
14	they are convinced of the efficacy as measured by
15	protein expression levels, and safety profile is
16	good, then they will put the package together and
17	file an IND, and try to get into a phase 1 where
18	they give it to healthy patients, make sure it's
19	safe.
20	Q In terms of from the viewpoint of a
21	medicinal chemist, assembling these therapeutics,
22	these oligonucleotides, generally speaking, the
23	medicinal chemist isn't the one that's involved in
24	creating the individual building blocks, though,
25	correct?

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1	A No, they are. I mean, definitely wouldn't
2	be a competent medicinal chemist if you didn't know
3	how like, if you were only able to make things
4	where you could buy the building blocks, that would
5	be a pretty pretty sad medicinal chemist.
6	Q Just going back to the, you know,
7	definition here. What if there was a chemist that
8	was an expert in synthesizing the building blocks;
9	that that was their the chemist's focus was for
10	years, two to three years or even more, expertise at
11	synthesizing the building blocks, but they knew
12	nothing about medicinal chemistry, would that person
13	be a POSA, in your under your definition?
14	A I mean, it's really a strange
15	hypothetical. I don't know anybody like that. I've
16	never heard of anybody like that. It would be a
17	very sad intellectual human who would devote their
18	life to making oligonucleotide building blocks, but
19	not have any interest in how they are used.
20	So I've never met anybody like that in
21	companies that just knows how to make a sugar but
22	doesn't know what it's used for, or why certain
23	building blocks are employed in certain cases. So
24	it's a strange hypothetical, but I'm happy to
25	entertain it.

1	If the purpose was, you know, let's find
2	the building block in this particular case, they
3	would look and they would find that building block,
4	let's say in the Aerschot example or the '596
5	example, and they would say, oh, here's a building
6	block. And they would use that to make, you know,
7	the key intermediate used for whatever their oligo
8	synthesis regime would be.
9	So it doesn't take a tremendous amount of
10	skill to do a first initial pass to scan the
11	literature for what is known.
12	Q So if I don't know if I characterized
13	the chemist the way you characterized it in my
14	hypothetical.
15	But what if there is a chemist that was an
16	expert at synthesizing just these building blocks,
17	maybe they were aware of, you know, the ultimate
18	therapeutic, you know, and they care about that as a
19	human being, but they are not a medicinal chemist,
20	but they understand that what they are doing is part
21	of a project that involves medicinal chemistry, but
22	they don't have the expertise that a medicinal
23	chemist would have to apply this product to a
24	therapeutic. Would they qualify as a POSA under
25	your definition?

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1	A Well, I'm not going to sort of this is
2	a weird, very weird hypothetical. But I think there
3	is too much compartmentalization going on. That's
4	not how drug discovery works.
5	So there's people who you know, the
6	medicinal chemist is usually the synthetic
7	organist chemist in general is usually the sole
8	person on the project who knows the most about
9	everything. So they know how to make the building
10	blocks, they know how to make stuff. You know, all
11	pharma companies are making products that are
12	chemicals.
13	So they are the ones that are they are
14	the creators, and they work with the biologists hand
15	in hand on the assays, they know what their target
16	product profile is supposed to look like in terms of
17	efficacy and the various liabilities they want to
18	try to solve by making analogs of them. And so it's
19	a very a weird hypothetical to have someone who
20	only knows how to make building blocks, but has no
21	idea about the when and where and why of how those
22	building blocks are used.
23	So, yeah, would they fall into this
24	definition? I don't know. It's sort of a weird
25	hypothetical. I mean, I'll stick with what I've got

1	written here. I mean, if you want to take your
2	hypothetical chemist who doesn't know medicinal
3	chemistry, but only knows how to make building
4	blocks, and ask a specific instance of would they
5	know this or would they know that, we can go further
6	on that.
7	But, yeah, they might be a POSA in certain
8	cases. I mean, it just depends on what you are
9	asking, like, what's the problem you are asking them
10	to solve. You know what I mean?
11	Q Yeah. So I just want to be clear as to
12	what your viewpoint in the definition is. And it
13	says here, medicinal chemistry, synthetic organic
14	chemistry, and nucleic acid chemistry.
15	And so the way this is written, it seems
16	that all of those experience in all of those
17	areas are required under your definition, and I'm
18	just confirming if that is what your testimony is.
19	A I mean, to some extent I've seen chemists
20	who didn't necessarily know they didn't
21	practice I've had students who were experts in
22	synthetic organic chemistry, knew a lot about
23	medicinal chemistry, hadn't really focused in the
24	area of nucleic acid chemistry and then gone on to
25	companies that engage in nucleic acid chemistry, and

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1	they were hired because if, you know, if you're a
2	really, really talented synthetic organic chemist,
3	learning the various aspects of the application part
4	are much easier to teach.
5	So companies usually want to hire people
6	who are really talented organic chemists because
7	they know that learning the other stuff doesn't take
8	as much time. So a good Ph.D. student from my
9	group, for example, had maybe worked on a project
10	that had nothing to do with nucleic acids, could
11	easily go to a company like Alnylam or Moderna, and
12	within a few weeks would be running circles around
13	people because they would be so good at chemistry,
14	and it would be very simple for them to use their
15	skills to apply it to the area of nucleic acid. So
16	maybe that addresses the question.
17	Q I'm not really sure I got an answer. And
18	I just want to know if one must be a medicinal
19	chemist or have experience in medicinal chemistry in
20	order to be a POSA under your definition, that's
21	what my question is.
22	A I mean, I don't want to revise the
23	testimony. It is what's written here. But, sure,
24	there's exceptions to this that you know, it's
25	malleable, I believe other definitions were

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1	proposed, and I had no problem with them as well.
2	It's a pretty straightforward set of
3	chemistries that is in these various cases we have
4	been talking about. So, you know, I suppose the
5	definition could be malleable on a case-by-case
6	basis depending on who the chemist is.
7	MR. SHORES: All right. I think if we can
8	take a break, a short break, come back on.
9	(Recess 1:52 p.m 2:04 p.m.)
10	BY MR. SHORES:
11	Q Dr. Baran, we want to pull we were just
12	looking at Exhibit 1003 from the '707 IPR. I would
13	like to look now
14	MR. SHORES: I'm sorry, what were we
15	looking at before I'm sorry, Court Reporter, what
16	did we have up before?
17	Q Okay. This is Exhibit 1001 from the '707
18	patent and we were looking at paragraph 20 of this
19	declaration.
20	Do you recall, Dr. Baran?
21	A Yes, sir.
22	Q Okay. And if we could pull up Exhibit
23	1001 1003 from the '569 patent.
24	Dr. Baran, have you seen this document
25	before?

1	A Yes.
2	Q What is this document?
3	A This is my declaration regarding the '569
4	patent and the (indiscernible) thereof.
5	Q Thank you.
6	And if you could refer to paragraph 21,
7	which is on page 6 of this document.
8	A 6, paragraph 21. Okay. I'm there.
9	Q Okay. And if you see there paragraph 21
10	states, "In my opinion, a POSA would have had a
11	Ph.D. (or equivalent degree) in organic or medicinal
12	chemistry and two to three years of postgraduate
13	work experience in medicinal chemistry, synthetic
14	organic chemistry, and nucleic acid chemistry,
15	including the development of oligonucleotide
16	therapeutics, diagnostics, or building blocks."
17	Did I read that correctly?
18	A Yes.
19	Q And that testimony is the same as the
20	testimony that was provided in the Exhibit 1003 of
21	the '707 patent?
22	A Looks like it, yeah.
23	Q And then the second sentence of paragraph
24	21 of Exhibit 1003 from the '569 patent says, and
25	I'll read that into the record, "Alternatively,
Transcript of Phil S. Baran, Ph.D. Conducted on January 22, 2024

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1	someone who had at least three years of work				
2	experience in these fields and who had gained a				
3	thorough understanding of the development of nucleic				
4	acid-based materials would also have qualified as a				
5	POSA with a bachelor's or master's degree in organic				
6	chemistry or medicinal chemistry."				
7	Did I read that correctly?				
8	A Yes.				
9	Q And is that the same testimony that is				
10	reflected in paragraph 20 of the Exhibit 1003 from				
11	the '707 proceeding?				
12	A I guess so. I'm assuming so.				
13	Q And then the last sentence says, of				
14	paragraph 21 of Exhibit 1003 of the '569 patent, the				
15	last sentence of paragraph 20 says, "As of September				
16	6th, 2008, I was a person of at least ordinary skill				
17	in the art as set forth above."				
18	Do you see that?				
19	A Yes.				
20	Q And what is the basis for that statement?				
21	What sorry. What was the basis for that				
22	statement?				
23	A Well, I have a tremendous amount of				
24	experience in medicinal chemistry, synthetic organic				
25	chemistry, consulted at numerous companies working				

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1	in the area of nucleic acid chemistry. So was well
2	aware of the challenges of the field. I taught
3	nucleic acid synthesis in class.
4	So, yeah, I would consider myself at least
5	to be a person of ordinary skill in the art at that
6	time.
7	Q And then if you remember that sentence,
8	"As of September 6th, 2008, I was a person of at
9	least ordinary skill in the art as set forth above,"
10	and then if we go to the previous exhibit, if we can
11	go to Exhibit 1003 from '707, paragraph 20, that
12	sentence does not appear as part of your testimony
13	in connection with paragraph 20 for Exhibit 1003 in
14	the '707 patent; is that correct?
15	A It doesn't look like it's there.
16	Q Is that an omission or were you not a
17	person of ordinary skill in the art in connection
18	with the '707 patent in the 2008 time frame?
19	A I don't know why that sentence is missing,
20	but I would still offer to put the same sentence
21	back in there.
22	Q Maybe I'll ask the question, which is
23	precise wordsmithing sentences and declarations, and
24	we understand there is a lot of materials in there.
25	As of in the 2008 time frame, your

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1	testimony in connection with the '707 patent is that
2	you were a person of at least ordinary skill in the
3	art as set forth above in paragraph 20; is that
4	correct?
5	A Yes.
6	Q Thank you.
7	And with respect to your with respect
8	to your publications, we talked about in the last
9	deposition in the '885 in the patent proceedings,
10	the IPR involving the '885 patent, we talked about
11	your some of your literature.
12	Do you recall that testimony?
13	A Yes.
14	MR. SHORES: Okay. And if we can pull up
15	Exhibit I think it might be currently listed as
16	2009, and we would want to mark as 2045, and that's
17	the deposition transcript from the '885 from the
18	deposition in the '885 proceeding.
19	(Exhibit 2045 marked for identification.)
20	MR. SHORES: So it should be listed as
21	Exhibit 2009 maybe in the
22	THE TECHNICIAN: Yes, would you like
23	that
24	MR. SHORES: marked as 2045.
25	THE TECHNICIAN: Okay.

1 MR. SHORES: Yeah. Thank you. 2 BY MR. SHORES: 3 And I've -- this exhibit, you see this Q 4 exhibit on the screen, Dr. Baran? 5 Yes, sir. Α 6 And this is a deposition transcript Q 7 relating to the '885 patent that was conducted 8 September 13th, 2023. 9 Do you have any reason to doubt this? 10 Α No, not at all. 11 Okay. And so if we go to page 75 of this, 0 12 I think it's -- yeah, page 75. 13 Do you agree that only about 14 of the over 250 papers that you published relates to 14 15 oligonucleotide synthesis? 16 Yeah, as of that date. Α 17 Ο Okay. 18 MR. SHORES: You can take the exhibit down. 19 20 Q Okay. So you've published over 250 21 papers, correct? 22 Α Yes. 23 Q And around -- at that time, in September, 24 around 14 or, you know, 14 or more papers related to 25 oligonucleotides, correct?

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A Approximately, yes.
Q And as we covered earlier today, you know,
several of those papers are focused on, you know,
P(V) the $P(V)$ chemistry that you championed,
right?
A Yes.
Q And have you ever published a paper that
is related to the synthesis of a phosphoramidite?
A There may be something in the papers. I'm
not sure. But for certain, I have consulted on this
topic on multiple occasions and taught it in class.
I think looking at papers is just one
myopic way of trying to pitch and hold one's
expertise. One doesn't reach my level by not having
expertise in something as fundamental and
foundational to the field of organic chemistry as
oligonucleotide synthesis.
So I've consulted on it for years, taught
classes on it. Certainly well aware of the area as
of the 2008 time frame, regardless of whatever the
publications are.
Q Yeah, I'm not trying to pigeonhole you.
I'm trying to understand the work that you've
conducted in connection with the synthesis of
building blocks. So that's the purpose of of my

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1	inquiry here.
2	Have you ever published a paper that
3	relates to the synthesis of, you know, building
4	blocks that go into the oligonucleotides?
5	A Generally those are too simple. Our lab
6	is really focused on far more complicated things.
7	So the synthesis of basal nucleotide
8	building blocks is pedestrian, and honestly, below
9	that of the capabilities of our lab.
10	And so I think that your intent, though,
11	based on what you've written after the deposition,
12	is indeed to try to invalidate me as a POSA or cast
13	shade in some light, and I understand that's your
14	job; it's wonderful. But it's a a tactic which
15	is, while legal, it's probably not morally right.
16	So I'm stating the fact that, yeah, I'm a
17	POSA of that date. This chemistry is quite simple
18	and beneath the skills of our group. It's
19	pedestrian science, to be honest.
20	MR. SHORES: Okay. I have no further
21	questions at this time.
22	MR. EDWARDS: A couple, maybe just one.
23	EXAMINATION
24	MR. EDWARDS:
25	Q Dr. Baran, what, if anything, do you stand

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1	to gain if any of the claims of the '707 and/or '569
2	patents are invalidated in this proceeding?
3	A Nothing at all.
4	MR. EDWARDS: I have no more questions.
5	MR. SHORES: No questions.
6	(Time noted: 2:17 p.m.)
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1	CERTIFICATE OF CERTIFIED SHORTHAND REPORTER
2	NOTARY PUBLIC
3	
4	I, MONIQUE VOUTHOURIS, Certified Court
5	Reporter and Notary Public within and for the State
6	of New Jersey, do hereby certify:
7	That PHIL S. BARAN, PH.D., the witness
8	whose deposition is hereinbefore set forth, was duly
9	sworn by me before the commencement of such
10	deposition, and that such deposition was taken
11	before me and is a true record of the testimony
12	given by such witness.
13	I further certify that the adverse party,
14	SHANGHAI HONGENE BIOTECH CORPORATION, was
15	represented by counsel at the deposition.
16	I further certify that the deposition of
17	PHIL S. BARAN, PH.D. occurred remotely on Monday,
18	January 22, 2024, commencing at 8:05 a.m. to 2:15
19	p.m. EST.
20	I further certify that I am not related to
21	any of the parties to this action by blood or
22	marriage, I am not employed by or an attorney to any
23	of the parties to this action, and that I am in no
24	way interested, financially or otherwise, in the
25	outcome of this matter.

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1	IN WITNESS WHEREOF, I have hereunto set my	
2	hand this 26th day of January 2024.	
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4	JOUTANY S	
5	Monque Vouthours	
6		
7	Monique Vouthouris, CCR, RPR, CRR	
8	Notary Public of the State of New Jersey	
9	My commission expires: April 8, 2024	
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