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Transcript of Phil S. Baran, Ph.D.

Date: February 20, 2024

Case: Shanghai Hongene Biotech Corporation -v- Chemgenes Corporation (PTAB)

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CHEMGENES EXHIBIT 2035
Shanghai Hongene v. ChemGenes
Case IPR2023-00490

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 IPR2023-00490

12 U.S. Patent No. 9,884,885 B2

13
14
15 CONTAINS PROTECTIVE ORDER MATERIAL

16 OUTSIDE ATTORNEYS' EYES ONLY

17 VIDEOTAPED DEPOSITION OF

18 PHIL S. BARAN, PH.D.

19 Conducted Virtually

20 Tuesday, February 20, 2024

21 8:03 a.m. EST

22
23 Job No.: 525629

24 Pages: 1 - 161

25 Reported by: Monique Vouthouris, CCR, RPR, CRR

1 VIDEOTAPED DEPOSITION OF PHIL S. BARAN,
2 PH.D., pursuant to notice, conducted virtually via
3 Zoom Videoconference, before Monique Vouthouris,
4 Certified Court Reporter, Registered Professional
5 Reporter, Certified Realtime Reporter, and Notary
6 Public in and for the States of New Jersey and
7 New York.

A P P E A R A N C E S

ON BEHALF OF PETITIONER SHANGHAI HONGENE
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8 JACOB BALISTRERI, Planet Depos Videographer

9 JACK DUNN, Planet Depos Technician

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E X H I B I T S

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96:22 - 159:11

P R O C E E D I N G S

THE VIDEOGRAPHER: Here begins Media
Number 1 in the continued videotape deposition of
Phil S. Baran, Ph.D., in the matter of Shanghai
Hongene Biotech Corporation versus ChemGenes
Corporation, PTAB, in the United States Patent and
Trademark Office before the Patent Trial and Appeal
Board, Case Number IPR2023-00490, U.S. Patent No.
9,884,885 B2.

Today's date is February 20 of 2024 and the
time on the video monitor is 8:03 a.m. The remote
videographer today is Jacob Balistreri representing
Planet Depos.

All parties of this video deposition are
attending remotely. Would counsel please
voice-identify themselves and state whom they
represent.

MR. SHORES: Yeah. Dan Shores, outside
counsel for ChemGenes Corporation, along with me today
from my firm -- firm of Rothwell, Figg, is Adam
Nicolais. And then there are other representatives
from ChemGenes here as well, including Kevin O'Connor
and Jeremy Little.

MR. EDWARDS: This is Jeremy Edwards from
the Procopio law firm on behalf of Hongene and the

1	witness.	08:04:09
2	THE VIDEOGRAPHER: The court reporter today	08:04:21
3	is Monique Vouthouris representing Planet Depos. The	08:04:23
4	witness will now be sworn.	08:04:26
5	PHIL S. BARAN, PH.D.,	08:04:47
6	being first duly sworn or affirmed by the Notary,	08:04:47
7	testifies as follows:	08:04:54
8	EXAMINATION	08:04:54
9	BY MR. SHORES:	08:04:55
10	Q I can probably say La Jolla, California is a	08:04:57
11	lot warmer than it is in Boston right now, so...	08:05:02
12	A Oh, yeah.	08:05:06
13	Q Seem to like the warm weather, so that's	08:05:08
14	good.	08:05:08
15	A Oh, yeah.	08:05:09
16	Q Okay. So you're sworn in. You understand	08:05:09
17	you're under oath, right?	08:05:11
18	A Yes, Counsel.	08:05:13
19	Q And the court reporter will be making a	08:05:14
20	written record of all my questions and all your	08:05:17
21	answers, right? You understand that?	08:05:20
22	A Yes, sir.	08:05:23
23	Q And so I'm just going to run through these	08:05:23
24	ground rules that I've done the last couple times, so	08:05:26
25	bear with me here.	08:05:29

1	And you understand that the court reporter	08:05:30
2	cannot take down non-verbal gestures like head nods,	08:05:32
3	right?	08:05:38
4	A Yes, sir.	08:05:39
5	Q And so you agree to give all verbal answers	08:05:40
6	to all my questions?	08:05:42
7	A Yes, I do.	08:05:44
8	Q And you understand that petitioner's counsel	08:05:45
9	is entitled to make concise objections to my	08:05:53
10	questions, right?	08:05:57
11	A Yes, I do.	08:05:57
12	Q And you also understand that petitioner's	08:05:58
13	counsel is not allowed to make speaking objections or	08:06:02
14	coach you on your answers.	08:06:06
15	Do you understand?	08:06:07
16	A Yes, I do.	08:06:07
17	Q And you understand that petitioner's counsel	08:06:09
18	is not allowed to act as an intermediary, right?	08:06:12
19	A Yes, I do.	08:06:16
20	Q For example, counsel is not allowed to	08:06:18
21	interpret questions, decide what questions you should	08:06:22
22	answer, or help you formulate your answers while	08:06:25
23	testifying, right?	08:06:28
24	A Correct.	08:06:29
25	Q And unless counsel instructs you not to	08:06:29

1	answer, you must answer my questions regardless of	08:06:36
2	objections that counsel may make.	08:06:41
3	Do you understand that?	08:06:44
4	A Yes, I do.	08:06:44
5	Q Okay. Is there any reason why you feel	08:06:45
6	today you would not be able to provide full, truthful,	08:06:54
7	and complete testimony?	08:06:57
8	A No, not all.	08:06:58
9	Q And that's what you will do today?	08:07:00
10	A Of course, yes.	08:07:03
11	MR. SHORES: Okay. Jack, I guess the	08:07:09
12	technician, if you could please mark Exhibit -- one	08:07:11
13	second here -- 1003.	08:07:18
14	THE TECHNICIAN: Stand by.	08:07:25
15	MR. SHORES: If you could introduce that.	08:07:38
16	THE TECHNICIAN: And, yes, sharing, sharing	08:07:41
17	now.	08:07:42
18	MR. SHORES: Okay.	08:07:42
19	(Baran Exhibit 1003 marked for	08:07:42
20	identification.)	08:07:43
21	THE TECHNICIAN: And I'll give control to	08:07:43
22	the witness. And, Dr. Baran, just click for control.	08:07:45
23	Let me switch -- let me switch to that arrow setting,	08:07:54
24	one sec. Let go of your mouse for a second. That	08:07:59
25	will be easier.	08:08:01

1	Okay. Go ahead.	08:08:02
2	BY MR. SHORES:	08:08:04
3	Q So, Dr. Baran, this is petitioner's	08:08:04
4	previously marked Exhibit 1003, and it's your	08:08:08
5	declaration -- your original declaration submitted in	08:08:13
6	this matter. Is that your understanding?	08:08:16
7	A Yes, sir.	08:08:19
8	Q Okay. And so if you go to the end or near	08:08:25
9	the end, I guess, before your CV. Yeah, exactly, the	08:08:28
10	next -- yes, page 77, you see that statement there,	08:08:43
11	could you read that into the record, please?	08:08:49
12	A "I declare under the penalty of perjury	08:08:51
13	under the laws of the United States of America that	08:08:55
14	the foregoing is true and correct."	08:08:57
15	Q And then this is dated January 18, 2023;	08:08:59
16	correct?	08:09:04
17	A Yes.	08:09:04
18	Q And that's your signature?	08:09:04
19	A Yes.	08:09:05
20	Q Okay. Thank you.	08:09:06
21	MR. SHORES: If, Jack, you can take that	08:09:10
22	down. And then put up -- introducing Exhibit 1033,	08:09:13
23	and this will be the same -- the same drill.	08:09:21
24	THE TECHNICIAN: Yes, stand by.	08:09:26
25	(Baran Exhibit 1033 marked for	08:09:28

1	identification.)	08:09:40
2	THE TECHNICIAN: And click for control.	08:09:40
3	Q And have you seen this document before,	08:09:44
4	Dr. Baran?	08:09:47
5	A Yes, sir.	08:09:47
6	Q And what is this document?	08:09:48
7	A This is the reply declaration.	08:09:50
8	Q Submitted in the -- in this case, right?	08:09:53
9	A Correct.	08:09:56
10	Q Okay. And if -- similarly, if you could go	08:09:57
11	toward the end, I guess it's probably close to the	08:10:00
12	very end because your CV is not attached, page 62.	08:10:03
13	Could you read that last sentence into the	08:10:07
14	record, please?	08:10:12
15	A "I declare under the penalty of perjury	08:10:13
16	under the laws of the United States of America that	08:10:16
17	the foregoing is true and correct."	08:10:18
18	Q And this is dated January 19, 2024, correct?	08:10:21
19	A Yes, sir.	08:10:25
20	Q And that's your signature?	08:10:25
21	A Correct.	08:10:26
22	Q Okay. Thank you.	08:10:27
23	MR. SHORES: The technician can take it	08:10:28
24	down.	08:10:30
25	Q Thank you, Dr. Baran.	08:10:35

1	A	Sure.	08:10:37
2	Q	So there's a couple just, you know,	08:10:38
3		technical things I want to talk about, you, as the	08:10:40
4		expert here.	08:10:47
5		In a number of the references that we've	08:10:48
6		seen, there are -- there's reference to different	08:10:51
7		types of deprotection conditions, you know,	08:10:53
8		different -- different chemical conditions that are	08:10:57
9		being utilized, and one of those deprotection	08:11:00
10		conditions is methylamine.	08:11:07
11		Are you familiar with methylamine?	08:11:11
12	A	Methylamine, yeah.	08:11:13
13	Q	Methylamine, excuse me.	08:11:17
14	A	No worries.	08:11:17
15	Q	Methylamine. Again, I defer to your	08:11:18
16		expertise on pronunciation.	08:11:19
17		You don't seem to mind when your name might	08:11:21
18		not be pronounced correctly, but --	08:11:26
19	A	No problem.	08:11:28
20	Q	Okay. So is methylamine, would you -- would	08:11:28
21		you consider that to be, you know, like a strongly	08:11:32
22		basic, harsh, mild; how would you characterize	08:11:38
23		methylamine?	08:11:45
24	A	It's a basic amine and its strength can be	08:11:46
25		attenuated based on the solvent it's co-mixed with.	08:11:50

1	So, you know, you can temper the strength of amines	08:11:55
2	based on the solvent you dissolve them in.	08:12:03
3	For example, one -- one -- if you want me to	08:12:08
4	expound further or just end there?	08:12:12
5	Q Yeah, I would, if you would for my	08:12:14
6	indulgence.	08:12:19
7	A Sure. So, for example, ammonia is also a	08:12:20
8	basic amine and one of ChemGene's references they use	08:12:23
9	to cite degradation issues is the Kawasaki reference,	08:12:28
10	and what's interesting and I think educational about	08:12:34
11	that is that they are able to temper the strength or	08:12:38
12	attenuate it by using ethanolic solution of ammonia to	08:12:45
13	solve the problem of RNA-based degradation upon	08:12:49
14	deprotection.	08:12:52
15	So, yeah, amines -- amines can be -- their	08:12:53
16	relative strength in terms of how they react can be	08:12:57
17	modulated and that's an example of it.	08:13:01
18	Q So it's modulated by utilization of a	08:13:03
19	co-solvent?	08:13:07
20	A Correct.	08:13:08
21	Q And so if you compare methylamine with	08:13:09
22	ammonia, is that an apples-to-apples comparison in	08:13:16
23	terms of what is more basic and what isn't?	08:13:20
24	A Well, I mean, you can go and look at PKs and	08:13:23
25	different solvents of, you know, methylamine may have	08:13:28

1 a weaker or stronger relative basicity depending on 08:13:33
2 the solvent it's used in. 08:13:38
3 It generally is considered to be a little 08:13:40
4 more mild to use it, even though depending on the 08:13:42
5 solvent, methylamine can actually be a stronger, more 08:13:49
6 nucleophilic base. 08:13:53
7 Q So I guess, you know, in terms of the 08:13:57
8 comparison between methylamine and ammonia, would you 08:14:00
9 say that methylamine is less basic than ammonia or 08:14:04
10 more basic? 08:14:09
11 A Well, it depends on the pKa chart you look 08:14:10
12 at. But, you know, you'll find that the PK of 08:14:13
13 methylamine in some PK's measurements could be 08:14:18
14 stronger. 08:14:23
15 Q And what about methanolic ammonia as 08:14:25
16 compared to ammonia; I mean, is that -- what is the 08:14:30
17 difference between methanolic ammonia and ammonia? 08:14:34
18 A It's probably going to be slightly 08:14:39
19 attenuated relative to, let's say, a dissolving to use 08:14:42
20 neat ammonia, you can do that; temperature is low 08:14:46
21 enough, ammonia is a liquid. So having it in methanol 08:14:50
22 will attenuate its basicity because of hydrogen 08:14:54
23 bonding effects, for example. 08:14:58
24 Q And what effect does the methanol have; is 08:14:59
25 that the solvent that it's mixed with? 08:15:03

1	A	Yeah.	08:15:05
2	Q	Okay. So when you say neat, that reminds me	08:15:05
3		of scotch, so pardon me. So you can have ammonia,	08:15:09
4		neat ammonia --	08:15:13
5	A	Yeah.	08:15:14
6	Q	-- methanolic ammonia, and as compared	08:15:14
7		between neat ammonia and methanolic ammonia, is	08:15:18
8		methanolic ammonia less basic than ammonia neat?	08:15:22
9	A	It's probably going to be weaker, and the	08:15:26
10		other thing is the concentration will be lower.	08:15:30
11	Q	Gotcha. Okay. And you can -- depending on	08:15:33
12		the concentration, there's a lot of variables at play	08:15:36
13		there.	08:15:39
14		And then what about aqueous ammonia?	08:15:39
15	A	Well, that's stronger because now you've	08:15:43
16		some ammonium hydroxide that's being formed. So	08:15:50
17		there's some percentage of the water that's being	08:15:54
18		deprotonated and now you have hydroxide ion in there.	08:15:59
19	Q	So would you say it's -- is that more basic	08:16:04
20		than neat ammonia?	08:16:06
21	A	Well, it can be depending on the compound.	08:16:07
22		I mean, the effective -- the effective strength of it	08:16:11
23		can -- it can, depending on the functional group that	08:16:16
24		it's interacting with it, it can have more of an	08:16:19
25		ability to hydrolyze because now you've got hydroxide	08:16:23

1 in solution rather than just ammonia. 08:16:27

2 Q So head-to-head comparison between ammonia 08:16:30
3 and aqueous ammonia, which one is -- would be more 08:16:35
4 basic? 08:16:38

5 A In terms of -- well, it's complicated 08:16:39
6 because when you're thinking about basicity, what 08:16:41
7 you're really worried about in the terms of what we're 08:16:44
8 talking about is capacity to hydrolyze something or 08:16:46
9 deprotect something. And so the capacity to hydrolyze 08:16:50
10 with ammonium hydroxide is probably going to be 08:16:54
11 greater than just using ammonia directly. 08:16:58

12 Q So ammonia -- aqueous ammonia is ammonia 08:17:02
13 hydroxide? 08:17:07

14 A There's a lot of ammonium hydroxide in 08:17:08
15 there. 08:17:11

16 Q Right. It seems like a lot of different -- 08:17:11
17 different ammonium hydroxides out there in the 08:17:15
18 literature. 08:17:19

19 So you're saying that -- 08:17:21

20 (Court Reporter clarification.) 08:17:21

21 Q So you're saying that aqueous ammonia versus 08:17:28
22 ammonia, aqueous ammonia, can be more basic than 08:17:33
23 ammonia? 08:17:38

24 A I'm saying that now you've got hydroxide, so 08:17:39
25 the hydroxide is going to be better at hydrolyzing 08:17:45

1	than just pure ammonia.	08:17:49
2	Q Right. But I guess -- I guess my question	08:17:53
3	was whether, you know, when you stack them up head to	08:17:56
4	head, it's not in the -- I'm just trying to understand	08:17:58
5	the difference in the science here.	08:18:01
6	So you've got ammonia and you've not aqueous	08:18:04
7	ammonia. So putting aside the variables, you know,	08:18:09
8	but if you had stacked them up head to head, you know,	08:18:12
9	from a scientific perspective, chemistry perspective,	08:18:16
10	which one would be more basic between ammonia and	08:18:20
11	aqueous ammonia?	08:18:24
12	A Well, it depends because you've got ammonia,	08:18:25
13	and so the PK of that is about 9.2 or so. And then	08:18:32
14	the ammonium -- then you've got hydroxide. I'm going	08:18:42
15	to say, you know, by definition, the ammonia has to be	08:18:46
16	more basic because of C proteinating, it's able to	08:18:54
17	deproteinate the water.	08:18:59
18	However, in terms of reactivity towards	08:19:01
19	hydrolyzing something, the hydroxide is generally more	08:19:05
20	adept at hydrolyzing esters and amides than just neat	08:19:07
21	ammonia. And that's why, one, for convenience reason	08:19:12
22	because ammonia is a gas at room temperature, and two,	08:19:16
23	the oxygen nucleophile is better at doing the	08:19:19
24	hydrolysis. So that's why people will use ammonium	08:19:23
25	hydroxide or ammonia in methanol, that kind of thing.	08:19:27

1	But from a first principle standpoint, the	08:19:31
2	ammonia is deproteinating the water so it has to be	08:19:34
3	more basic.	08:19:38
4	Q And again, as compared to -- so those are, I	08:19:42
5	guess, different flavors of ammonia, right?	08:19:44
6	We've got ammonia, methanolic ammonia.	08:19:47
7	Methanolic I think you said was a co-solvent that's --	08:19:51
8	right? There's a solvent that's co-mixed with the	08:19:54
9	ammonia and methanolic ammonia. And then aqueous	08:19:58
10	ammonia is similar.	08:20:03
11	So those are different flavors of ammonia,	08:20:04
12	right? You've got ammonia, neat ammonia, and then	08:20:06
13	you've got a variety of ammonia with other, you know,	08:20:08
14	solvents mixed with the ammonia, right, to get those	08:20:13
15	flavors?	08:20:17
16	A Yes.	08:20:18
17	Q And then you've got methylamine.	08:20:18
18	A Methylamine, which is slightly more basic	08:20:21
19	even than ammonia because you've got that alkyl group	08:20:24
20	on it that adds basicity.	08:20:28
21	Q Right. And you're familiar with the -- and	08:20:31
22	do you have a sense about, like, if you were -- if you	08:20:32
23	were to have these on the shelf, like say you had	08:20:35
24	methylamine and ammonia on the shelf --	08:20:40
25	A Yeah.	08:20:43

1 Q -- and you were going to deprotect an 08:20:43
2 oligonucleotide, which one would you use for speed? 08:20:47

3 A I mean, it really -- I would, you know, have 08:20:55
4 a protocol that I would look at, and, you know, I 08:20:56
5 think you would have a set of protocols where some 08:21:01
6 people use ethanol amine, some people use methylamine, 08:21:04
7 some people use ammonia. And you would follow the 08:21:11
8 general protocol with whatever your synthesizer is 08:21:13
9 loaded with. It might be methanolic ammonia. 08:21:16

10 For most cases, probably methylamine or 08:21:17
11 methanolic ammonia is just fine. And in specialized 08:21:21
12 cases you might change the stock solution and the 08:21:25
13 oligo synthesizer to be something that's more in line 08:21:29
14 with whatever specific application you've got. But 08:21:33
15 these days, methylamine ammonia is pretty much 08:21:39
16 standard fair. 08:21:44

17 Q And why -- you said methylamine ammonia, 08:21:46
18 does that mean -- 08:21:49

19 A Or ammonia, yeah. 08:21:50

20 Q Standard fair. 08:21:51

21 A Yeah. 08:21:52

22 Q But methylamine is more basic than ammonia. 08:21:53

23 A I mean, it depends on the table you look at. 08:21:58
24 But in general, it's like a PK unit more basic or 08:22:01
25 less; it's close. 08:22:07

1	Q	Are you familiar with Reddy's work with	08:22:11
2		methylanine?	08:22:15
3	A	I have to see the reference you're talking	08:22:17
4		about.	08:22:19
5	MR. SHORES:	Okay. Can we pull up Exhibit	08:22:21
6		1040.	08:22:23
7	THE TECHNICIAN:	Stand by.	08:22:30
8	MR. SHORES:	So this is one of the exhibits	08:22:31
9		that you considered in this case.	08:22:32
10	THE TECHNICIAN:	Counsel, I'm just looking.	08:22:42
11		I don't have it from the most recent, so I'm just	08:22:44
12		looking back through the previous. Give me a second	08:22:47
13		here.	08:22:49
14	MR. SHORES:	Okay.	08:22:50
15	THE TECHNICIAN:	And you did say 1040. I	08:22:58
16		don't see a 1040.	08:23:00
17	MR. SHORES:	Okay. That would be a --	08:23:02
18	MR. NICOLAIS:	Yeah, this is Adam Nicolais.	08:23:08
19		Just one second. It was in there last night. I'm not	08:23:10
20		sure what happened. So just give me a second.	08:23:13
21	THE TECHNICIAN:	Oh, I see it. I'm sorry.	08:23:13
22		It's named a little differently. I got it now. Stand	08:23:15
23		by.	08:23:22
24		(Baran Exhibit 1040 marked for	08:23:22
25		identification.)	08:23:22

1	BY MR. SHORES:	08:23:41
2	Q Okay. Dr. Baran, you see this exhibit here?	08:23:41
3	A Yup.	08:23:45
4	Q And you've seen it before?	08:23:46
5	A Yes, mm-hmm.	08:23:51
6	Q And what is this exhibit?	08:23:53
7	A This is a paper where they look at various	08:23:54
8	cytosines with acetyl groups on it and talk about, you	08:23:58
9	know, relatively fast deprotection and cleavage of the	08:24:04
10	acetyl group.	08:24:08
11	Q Okay. If you can go to page 2.	08:24:11
12	A This page?	08:24:18
13	Q Yes. Yeah, I guess that, too.	08:24:20
14	Actually, page 3 of the -- so it would be	08:24:33
15	1590. And you see the second full paragraph that	08:24:39
16	starts with "As the data"?	08:24:44
17	A Oh, sorry. Okay. Yeah.	08:24:45
18	Q Yeah. Could you read that sentence into the	08:24:47
19	record please?	08:24:50
20	A "As the data in Table 2 [sic] show,	08:24:51
21	methylamine/ammonium hydroxide is much faster than	08:24:54
22	ammonium hydroxide in deprotecting oligonucleotides."	08:25:01
23	Keep going?	08:25:06
24	Q No. That's okay. And then if you can look	08:25:07
25	at Table 2 -- or Table 1 of the following page, which	08:25:09

1	is on page 1591 of the article.	08:25:14
2	A Okay.	08:25:18
3	Q And you see the results there under Table 1?	08:25:18
4	A Yes, mm-hmm.	08:25:21
5	Q And you see the results also under Table 2	08:25:22
6	that say "Time required for complete deprotection of	08:25:27
7	oligonucleotides"?	08:25:31
8	A Yes.	08:25:32
9	Q So reading page 3, you know, where it says,	08:25:32
10	"As the data in Table 1 show, methylamine/ammonium	08:25:37
11	hydroxide is much faster than ammonium hydroxide" --	08:25:42
12	(Court Reporter clarification.)	08:25:59
13	Q So, Dr. Baran, if you look at, you know, in	08:26:00
14	looking at Table 1 and Table 2 on page 1591 of Exhibit	08:26:03
15	1040, and then looking at the statement on page 1590,	08:26:09
16	it says, "As the data in Table 1 show,	08:26:18
17	methylamine/ammonium hydroxide is much faster than	08:26:22
18	ammonium hydroxide in deprotecting oligonucleotides,"	08:26:26
19	do you agree with that statement?	08:26:33
20	A Yeah.	08:26:34
21	Q Okay. And so if we go to --	08:26:35
22	MR. SHORES: You can take the exhibit down.	08:26:45
23	Q So if we're talking about ammonia, would you	08:26:53
24	characterize that as a harsh deprotection condition?	08:26:56
25	A I mean, it really -- I mean, it depends,	08:27:03

1 like, on the scenario. Is it harsh? It's a relative
2 term. So in some cases, ammonia is not harsh if there
3 are no functional groups that are offended by it or
4 decomposed by it.

5 So if you've got an oligonucleotide
6 structure that really has no -- no issues in terms of
7 stability, then ammonia add mixed with water to give
8 ammonium hydroxide with extended exposure time may not
9 be a problem at all.

10 But obviously, there are use cases where you
11 want to speed that up. And adding things like
12 ethanolamine or methylamine or other -- many amines
13 that have been explored in literature can lead you to
14 a faster deprotection, that while the reagent might be
15 a little more harsh, the exposure time is long --
16 shorter, rather, and that leads to the overall effect
17 of being more mild because the exposure time is
18 shorter.

19 Q Exposure time to -- you're talking about in
20 a particular use case?

21 A Yeah. The exposure time -- like in organic
22 chemistry, sometimes it's useful to have what you
23 would call a more harsh or strong reagent, but with a
24 shorter exposure time has the effect of being less
25 harsh even though the reagent itself is more potent.

1	Does that make sense?	08:28:42
2	Q I guess so. You know, what -- I'm just	08:28:44
3	looking for your opinion relative to how -- you know,	08:28:46
4	the comparison between ammonia and, you know,	08:28:51
5	methanolic ammonia and aqueous ammonia and	08:28:58
6	methylamine. And I'm not sure -- I mean, you've	08:29:03
7	testified to certain aspects of that, but you're also	08:29:07
8	sounds like you're saying it depends.	08:29:11
9	So you can't really give a clear answer on	08:29:13
10	any of that?	08:29:17
11	A Well, I'm not sure what exactly the question	08:29:17
12	is. Can you state what the question is?	08:29:19
13	Q Yeah, pretty -- these are like real -- I	08:29:22
14	mean, it's just out of the context of the case, just	08:29:24
15	as in your experience as an organic chemist, if you	08:29:26
16	were to have ammonia on, you know, on one hand and you	08:29:32
17	have methylamine on the other, which one is more	08:29:38
18	basic?	08:29:43
19	A Well, I answered that question already.	08:29:44
20	Methylamine, if you just look at a pKa table, is more	08:29:46
21	basic than ammonia. That I've told you already, so.	08:29:50
22	But when you do a reaction in organic chemistry, the	08:29:53
23	context matters, because usually you're dealing with A	08:29:57
24	plus B goes to C. And in this case you've told me	08:30:00
25	what A is, which is an amine of some sort, but I don't	08:30:03

1	know what B is, and that matters because it tells you	08:30:07
2	about the -- what you're going to get in C.	08:30:10
3	So if you want to talk about a specific case	08:30:13
4	of an oligonucleotide, where if you define that as B,	08:30:16
5	we can have a more fulsome discussion. But if you	08:30:21
6	just want the general question of is ammonia more	08:30:24
7	basic or less basic than methylamine, then the answer	08:30:27
8	is go look at a pKa table and you'll find that	08:30:29
9	methylamine is more basic than ammonia.	08:30:32
10	Q Okay. Thank you, Dr. Baran.	08:30:35
11	A Sure.	08:30:52
12	MR. SHORES: Okay. If we can pull up	08:31:00
13	Exhibit 1033.	08:31:03
14	Q And this is Exhibit 1033, Dr. Baran, we	08:31:19
15	looked at this earlier, this is your reply declaration	08:31:26
16	in this case, right?	08:31:28
17	A Yes, sir. Mm-hmm.	08:31:29
18	Q Okay. If we can go to paragraph 16 of this	08:31:30
19	declaration.	08:31:36
20	A Okay.	08:31:39
21	Q And here you provide a description of your	08:31:40
22	understanding of the lead compound analysis framework;	08:31:50
23	is that correct?	08:31:55
24	A Yes.	08:31:55
25	Q Is it correct that you did not apply the	08:31:56

1	lead compound analysis in your opening declaration?	08:32:04
2	A I don't think the lead compound analysis is	08:32:11
3	relevant to this case at all.	08:32:16
4	Q I understand that based on your testimony.	08:32:21
5	But I'm asking if, in your opening declaration, did	08:32:25
6	you apply the lead compound analysis?	08:32:29
7	A I mean, as I recall, we would have to go	08:32:31
8	look at the -- I would have to go look at the -- that	08:32:35
9	initial declaration, it was, I don't know, a hundred	08:32:41
10	page or something. I'm sure it's mentioned in there.	08:32:42
11	But I think the key conclusion is that a lead compound	08:32:45
12	analysis is irrelevant when you're talking about	08:32:48
13	reagents, not -- nobody applies a lead -- no one	08:32:52
14	thinks about a lead compound when they're picking a	08:32:57
15	building block.	08:33:01
16	MR. SHORES: Okay. If we can pull up	08:33:02
17	Exhibit 1003, please.	08:33:05
18	THE TECHNICIAN: On screen.	08:33:11
19	Q And is this your -- you mentioned earlier --	08:33:16
20	you just mentioned, you just testified, Dr. Baran,	08:33:19
21	that you believe that a lead compound analysis was	08:33:24
22	mentioned -- may have been mentioned in your opening	08:33:28
23	declaration, right?	08:33:32
24	A I would have to check. I mean, if you want	08:33:34
25	to direct me to a page --	08:33:37

1	Q	Well, it's not there. I actually cannot --	08:33:41
2		cannot point you to a page that talks about lead	08:33:44
3		compound. But if you want to look at the legal	08:33:48
4		section --	08:33:51
5	A	If you tell me there's no lead compound, or	08:33:52
6		if you want me to spend the time to go through the	08:33:54
7		hundred pages, I can do that. Or if you just want to	08:33:58
8		tell me there's no lead compound in here, that's fine.	08:34:00
9	Q	So it's your testimony that you did not	08:34:03
10		apply -- apply the lead compound analysis in your	08:34:05
11		opening declaration, correct?	08:34:07
12	A	Well, my testimony is I didn't memorize this	08:34:09
13		declaration. So if you tell me it's not mentioned in	08:34:13
14		here, if I can do a word search, then I believe you.	08:34:17
15		But otherwise, I'm going to go through and see if I	08:34:20
16		can find -- I can't search on here, I don't know if	08:34:24
17		there's a way to search for the word "lead compound"	08:34:27
18		we can or --	08:34:30
19	MR. SHORES:	Jack, Jack, is there a way to	08:34:31
20		do that?	08:34:33
21	A	Oh, here, "lead." It looks like it's not in	08:34:34
22		here, so, the word "lead." It's searching. No.	08:34:40
23		I'm satisfied that there's no lead compound	08:34:49
24		in here.	08:34:51
25	Q	Okay. So, therefore, you did not apply the	08:34:52

1	lead compound analysis in your opening declaration,	08:34:54
2	correct?	08:34:56
3	A It appears not.	08:34:57
4	Q Okay.	08:35:00
5	MR. SHORES: So if we can go back to Exhibit	08:35:01
6	1033.	08:35:03
7	THE TECHNICIAN: On screen.	08:35:07
8	Q And just in terms of the lead compound	08:35:10
9	analysis, did counsel advise you about the lead	08:35:14
10	compound analysis in advance of your opening	08:35:18
11	declaration, which is the Exhibit 1003?	08:35:20
12	MR. EDWARDS: Object to form. Instruct not	08:35:23
13	to answer. Our communications are privileged.	08:35:25
14	MR. SHORES: Well, they're not privileged,	08:35:28
15	but -- are you asserting work product?	08:35:31
16	MR. EDWARDS: You have my objection and	08:35:37
17	instruction. Next question.	08:35:38
18	MR. SHORES: So what is the basis of your	08:36:05
19	objection? Because I -- it's not privileged. It's --	08:36:07
20	are you asserting work product?	08:36:12
21	MR. EDWARDS: I'm instructing the witness	08:36:14
22	not to answer --	08:36:15
23	MR. SHORES: On the basis of privilege?	08:36:17
24	MR. EDWARDS: -- privilege or work product,	08:36:18
25	whatever you want to call it. My communications with	08:36:19

1 the expert witness are not discoverable. He's 08:36:23
2 instructed not to answer your question asking him what 08:36:25
3 I advised him. 08:36:28

4 MR. SHORES: Well, that's an incorrect 08:36:30
5 statement of the law. But if you want to make that 08:36:32
6 assertion, we will take it under advisement. 08:36:39

7 BY MR. SHORES: 08:36:46

8 Q Dr. Baran, when did you first learn about 08:36:47
9 the lead compound analysis? 08:36:50

10 A I don't recall. 08:36:54

11 Q Well, it was at least as of your second 08:37:04
12 declaration here, Exhibit 1033, correct? 08:37:09

13 A I may have encountered this legal concept in 08:37:13
14 other cases I've worked on over the years. There's 08:37:17
15 the legal framework that is described in this 08:37:22
16 document, and then there's the common sense 08:37:26
17 interpretation of it, and the two are actually kind of 08:37:28
18 kind of similar. Like, when it was described to me, I 08:37:32
19 was, like, yeah, that's what a -- that's what a lead 08:37:36
20 compound is. 08:37:39

21 Q When you say when it was described to you, 08:37:42
22 when was that? 08:37:44

23 A That I don't -- I don't recall the date or 08:37:45
24 whether it was even this case. 08:37:48

25 Q Well, in this page 6, and we're looking here 08:37:54

1 right now at paragraph 16, it says, "In my opinion,
2 the 'lead compound' framework for assessing
3 obviousness, which has been explained to me by my
4 attorney" -- "by attorneys, is primarily relevant to
5 the field of drug discovery in the pharmaceutical
6 arena, where it pertains to the identification," blah,
7 blah, blah, right?

8 So you learned about the lead compound
9 framework in advance of submitting your reply
10 declaration, correct?

11 A Yeah. The question is whether that's the
12 first time I had heard of it. And --

13 Q Well, the question -- I'm sorry. Go ahead.

14 A That I don't know.

15 Q And here it says "which has been explained
16 to me by attorneys." Is that your present counsel?

17 A Yeah, in formulating this document, sure, we
18 had discussions on that.

19 Q And here it says "In my opinion, the "lead
20 compound" framework for assessing obviousness, which
21 has been explained to me by attorneys, is primarily
22 relevant to the field of drug discovery in the
23 pharmaceutical arena."

24 Did I read that correctly? Did I read that
25 correctly?

1	A	Yes.	08:39:31
2	Q	Okay. I didn't hear; I was looking at my	08:39:32
3		paper.	08:39:34
4	A	Oh, sorry.	08:39:34
5	Q	So you were advised that the lead compound	08:39:36
6		is primarily relevant to the field of drug discovery	08:39:45
7		in the pharmaceutical arena?	08:39:49
8		MR. EDWARDS: Object to form.	08:39:51
9	A	I mean, it could be -- a lead compound could	08:39:54
10		be in any area of discovery. It could be in	08:39:58
11		pharmaceutical, it could be agrochemistry, it could be	08:40:01
12		flavors and fragrances, it could be OLEDs, areas of	08:40:05
13		material science. I mean, writ large, the concept of	08:40:12
14		lead compound can be applied to many areas of	08:40:19
15		discovery chemistry, whether it's pharmaceutical or	08:40:22
16		otherwise. The sort of workflow of how a chemist goes	08:40:24
17		about identifying a lead compound is very similar in	08:40:31
18		different areas of society.	08:40:35
19	Q	And, you know, you're an accomplished	08:40:39
20		organic chemist, and is that coming from your	08:40:42
21		perspective of an organic chemist, or is that coming	08:40:46
22		from your understanding of what the law is?	08:40:49
23		Understanding you're not an attorney.	08:40:55
24	A	Yeah, I'm not an attorney. So the lead	08:40:56
25		compound framework, as it was described to me, is very	08:41:00

1	similar to the common sense definition that we organic	08:41:06
2	chemists use.	08:41:10
3	Q And would it surprise you to know that there	08:41:13
4	is a difference between the common sense definition of	08:41:18
5	what chemists use and what the law is?	08:41:20
6	A No, it wouldn't surprise me.	08:41:24
7	Q And in paragraph 16, you also say in the	08:41:29
8	last sentence, which is on page 7, you said "This	08:41:33
9	concept involves the assessment of structure,	08:41:36
10	activity, and utility of potential lead compounds in	08:41:38
11	the development of new drugs," correct?	08:41:42
12	Did I read that correctly?	08:41:45
13	A Yes.	08:41:47
14	Q Okay. And then below in paragraph 17, I	08:41:57
15	guess that's page 7 now.	08:42:01
16	A I'm trying to scroll down.	08:42:04
17	Q Yeah. Okay.	08:42:07
18	A There we go.	08:42:11
19	Q In here you say, "In contrast, in the field	08:42:11
20	of making reagents used in the production of	08:42:14
21	oligonucleotides as of 2009, the 'lead compound'	08:42:19
22	approach is not particularly informative or relevant."	08:42:22
23	Did I read that correctly?	08:42:26
24	A Yes.	08:42:28
25	Q So you seem to be drawing a line here	08:42:29

1 between reagents and lead -- and what you consider as 08:42:46
2 lead compounds, right? 08:42:52

3 A Well, necessarily so, because the 08:42:54
4 constituents of the whole are not the lead. It's the 08:42:58
5 whole that's the lead. 08:43:03

6 Q That -- but that is from the perspective of 08:43:06
7 a medicinal chemist, right, with its making -- it's 08:43:13
8 looking to make a therapeutic oligonucleotide, you're 08:43:17
9 -- are you saying that you view the oligonucleotide as 08:43:22
10 the lead? 08:43:26

11 A Of course it is. 08:43:29

12 Q Okay. If you had -- so that's from the 08:43:31
13 perspective of a medicinal chemist? 08:43:34

14 A It's a perspective for anyone that's working 08:43:38
15 on an oligonucleotide, whether it's a therapeutic 08:43:42
16 application or a diagnostic or whatever. Nobody in 08:43:48
17 their right mind would consider a reagent to be a lead 08:43:56
18 compound. It's nonsense. 08:44:01

19 Q It's nonsense from the perspective of a 08:44:04
20 scientist? 08:44:08

21 A Yeah. You could ask any -- any scientist 08:44:12
22 and point at their bottle of reagent and say, Is that 08:44:17
23 your lead compound? They would laugh at you. 08:44:21

24 Q If you had an oligonucleotide that wasn't 08:44:28
25 utilized for therapeutic purposes, that was used for, 08:44:31

1 I guess, you know, genetic research or, you know, what 08:44:38
2 are the other -- yeah, if you were a chemist 08:44:46
3 developing -- withdraw the question. That was a bad 08:44:51
4 question. 08:44:53

5 What if a chemist were to develop a new 08:44:53
6 oligonucleotide for genetic research purposes that's 08:44:59
7 not related to drug development, would -- would the 08:45:02
8 lead compound analysis apply to the oligonucleotide? 08:45:08

9 A Yeah, I already answered that. So for a 08:45:13
10 diagnostic or a tool, it's the same thing. You're 08:45:15
11 talking about the target, the lead is the whole 08:45:19
12 structure you're trying to make, not the individual 08:45:22
13 little building blocks that make it up. 08:45:25

14 Q So you're -- you're drawing a line as to 08:45:32
15 between an oligonucleotide, but you're saying that 08:45:36
16 building blocks are -- by definition, can never be a 08:45:40
17 lead compound? 08:45:46

18 A No. 08:45:48

19 MR. EDWARDS: Objection to form. 08:45:49

20 Go ahead. 08:45:51

21 A Not what I'm saying. So, for example, a 08:45:52
22 monomeric nucleotide can be a drug. And if the point 08:45:56
23 of the program -- and I think last deposition we spent 08:46:01
24 time on one such paper in that regard where they were 08:46:03
25 making antiviral compounds based on monomers. And if 08:46:09

1	you're making a monomeric nucleoside that is your drug	08:46:15
2	candidate, then -- then the monomers become your lead	08:46:19
3	compound.	08:46:23
4	But if you're working on an oligonucleotide,	08:46:23
5	it's in the name, oligo, then the constituents that	08:46:27
6	make up the oligo are not the lead; it's the whole	08:46:32
7	compound, the oligo part that is the compound.	08:46:36
8	Q So if you had an oligonucleotide -- we can	08:46:40
9	talk about, I guess, what you've testified to is that	08:46:46
10	the monomers with fluoro at the 2 prime position can	08:46:51
11	give an oligonucleotide increased binding affinity,	08:46:57
12	right?	08:47:03
13	A That is known in the literature.	08:47:03
14	Q So what if you had an oligonucleotide that,	08:47:07
15	you know, had -- I don't know, what would you say is	08:47:14
16	an -- is there an average size for an oligonucleotide	08:47:18
17	in terms of building blocks or monomers?	08:47:20
18	A No, you can't say there's an average size.	08:47:23
19	It depends on what type of oligo, what type of	08:47:26
20	application. They can be anywhere from 2 to many	08:47:30
21	hundreds.	08:47:33
22	Q Okay. Just to simplify things, if you had	08:47:34
23	an oligonucleotide that was, you know, 10 mers in	08:47:37
24	length --	08:47:41
25	A Okay.	08:47:41

1 given application? 08:49:45

2 A What does that mean, "inert"? 08:49:45

3 Q Okay. Could they be -- just have no 08:49:47

4 activity as it relates to the -- to the given 08:49:50

5 application? 08:49:54

6 A I don't even -- I don't understand what "no 08:49:57

7 activity" means. In the context of oligonucleotide -- 08:50:00

8 (Simultaneous speaking.) 08:50:03

9 Q Okay. Each one -- I'm sorry, go ahead. I 08:50:03

10 don't want to talk over you. 08:50:07

11 A In the context of an oligonucleotide, each 08:50:08

12 unit does something. There's -- the concept of 08:50:11

13 inertness doesn't make sense, because even if it -- I 08:50:14

14 know what you mean. But even if let's say a 08:50:18

15 hypothetical monomer were inert by whatever your 08:50:21

16 definition is, it can't be inert because it has a 08:50:25

17 spacing, there's a spacing there. So it has part of a 08:50:28

18 function. 08:50:31

19 So I don't know what "inert" means in an 08:50:32

20 oligonucleotide sequence, because at the very minimum, 08:50:35

21 it provides a spacing between the others. So there's 08:50:41

22 a function that's inherent which makes it -- which 08:50:44

23 makes it impossible for you to label one of those 08:50:47

24 monomers as being inert. 08:50:50

25 Q Right. But so it could serve as a spacer 08:50:52

1	and you're saying that serves a function in the	08:50:56
2	oligonucleotide in itself as a spacer?	08:50:58
3	A All of this is hypothetical.	08:51:00
4	Q Understood. Understood. And -- but in	08:51:02
5	terms of biological activity, would some of the	08:51:04
6	monomers have no biological activity when used as a	08:51:10
7	therapeutic?	08:51:17
8	A I don't know of a case like that. I mean, I	08:51:17
9	would have to look into that. I never heard of such a	08:51:23
10	scenario where you just sort of add a monomer to an	08:51:27
11	oligonucleotide that has no function whatsoever, no --	08:51:31
12	no activity at all. I've never heard of that.	08:51:35
13	Q Okay. So I guess I'm just trying to	08:51:40
14	understand and also, you know, ask my questions.	08:51:43
15	So if you had a 10 -- back to the 10 mer	08:51:46
16	oligonucleotide example, and you're designing that	08:51:51
17	oligonucleotide to have increased binding affinity,	08:51:55
18	your testimony is that one of a number of options	08:52:01
19	would be to use a 2-prime-fluoro building block,	08:52:05
20	right?	08:52:13
21	A Yeah, one of a number of options, or you may	08:52:13
22	not do it at all. I mean, it's just sort of an option	08:52:16
23	in the toolkit akin to small molecule drug discovery,	08:52:19
24	where, you know, the medicinal chemist has the option	08:52:25
25	to put flourine at different spots in the molecule or	08:52:28

1	chlorine at different parts of the molecule. It's an	08:52:32
2	option. They can put a sulfonamide. They can put a	08:52:36
3	pyridine ring. They can choose the building block	08:52:41
4	from their millions and millions of compounds that are	08:52:43
5	available and decide whether or not to incorporate it	08:52:45
6	into the lead compound. It's identical analogy.	08:52:48
7	Q So if you were to have -- you know, just to	08:52:53
8	define the hypothetical, because I know there's a lot	08:52:57
9	of different variables, but to define the	08:52:59
10	hypothetical, you're designing a 10 mer	08:53:01
11	oligonucleotide for increased binding affinity, you	08:53:04
12	use 2-prime-fluoro building blocks, and those building	08:53:09
13	blocks could be any number of those 10, right, the	08:53:17
14	2-prime-fluoro, you could have three 2-prime-fluoro	08:53:23
15	and then seven other building blocks, right?	08:53:26
16	A You could have anywhere from zero to 10 of	08:53:29
17	the 10 mer.	08:53:32
18	Q Right. You can even have a 10 mer all	08:53:33
19	2-prime-fluoro?	08:53:37
20	A Sure. Hypothetically, yeah.	08:53:38
21	Q Okay. So let's assume for this hypothetical	08:53:40
22	that the 10 mer building block has three monomers --	08:53:46
23	the 10 mer oligonucleotide has three 2-prime-fluoro	08:53:54
24	monomers for increased binding affinity, and then the	08:54:02
25	other seven are there, but they don't have anything to	08:54:05

1	do with binding affinity, they have to do with other	08:54:08
2	characteristics of the particular oligonucleotide.	08:54:11
3	Do you understand the hypothetical?	08:54:13
4	A I understand the hypothetical, but it's kind	08:54:15
5	of weird because all of them are going to have some	08:54:19
6	basal level of binding affinity. You wouldn't have a	08:54:22
7	case where your 10 mer oligo, just three of them are	08:54:26
8	binding and the other seven are there because they're	08:54:30
9	like some spinach. It doesn't work like that.	08:54:33
10	Q Okay. That's fair. All right. This is	08:54:36
11	your area, so.	08:54:38
12	But if I were to take that -- if I were to	08:54:38
13	take that -- or if you were to take that, or if one of	08:54:41
14	ordinary skill in the art were to take the -- that 10	08:54:44
15	mer oligonucleotide that has three 2-prime-fluoro for	08:54:49
16	purposes of increased binding affinity, and then you	08:54:55
17	were to take those -- those 2 prime -- three	08:54:59
18	2-prime-fluoros away and replace them with monomers	08:55:04
19	that aren't known to have increased binding affinity,	08:55:07
20	the overall binding affinity of the oligonucleotide	08:55:12
21	would decrease, correct?	08:55:18
22	A If you made the deliberate choice to	08:55:19
23	decrease binding efficiency by choosing building	08:55:21
24	blocks that would confer the overall lead compound or	08:55:25
25	oligonucleotide to have less binding, then you would	08:55:28

1	be successful, if that was your -- your goal.	08:55:31
2	Q But you would be successful by removing the	08:55:34
3	2-prime-fluoro monomers?	08:55:40
4	A You would have to try and see. I mean, that	08:55:43
5	would be one thing you could potentially do. But it's	08:55:47
6	all -- this hypothetical, and in this hypothetical	08:55:50
7	what you're asking is how do we make a weaker binder,	08:55:54
8	which in some cases may be what you want. And if you	08:56:00
9	wanted to deliberately make a weaker binder, maybe --	08:56:04
10	maybe you would choose building blocks that somehow	08:56:09
11	attenuate.	08:56:11
12	But the thing is, is you wouldn't know until	08:56:12
13	you make and try. You could make some educated	08:56:15
14	guesses as to -- based on the literature what might	08:56:18
15	increase in binding or decrease, but you don't know.	08:56:21
16	So in this hypothetical example of having	08:56:23
17	three fluorines, you may actually decrease binding	08:56:27
18	rather than increase by having too many of them.	08:56:29
19	That's the point. That's why it's not a lead	08:56:32
20	compound. A building block is not a lead compound	08:56:35
21	because you don't know the properties of the whole	08:56:37
22	until you make the whole. That's the problem.	08:56:40
23	Q But with like a phosphoramidite building	08:56:42
24	block, that delivers a 2-prime-fluoro monomer,	08:56:48
25	correct?	08:56:52

1	A	Yeah. That has nothing to do with what	08:56:53
2		we're talking about. But yes, that --	08:56:57
3		(Simultaneous speaking.)	08:56:57
4	A	Yeah, that reagent is what you would use, if	08:57:00
5		you're going to use phosphoramidite chemistry to	08:57:01
6		incorporate a monomer into a growing oligonucleotide,	08:57:05
7		that's the reagent you would use, correct.	08:57:08
8	Q	And it delivers the 2-prime-fluoro, which	08:57:11
9		has a biological effect of increasing binding	08:57:14
10		affinity, correct?	08:57:20
11	A	It can. But I'm sure if we looked, there	08:57:24
12		are cases where in certain -- in certain instances it	08:57:29
13		actually decreases or provides less desirable	08:57:34
14		properties. Because in the lead compound, in the	08:57:38
15		common sense definition, it's more than just one	08:57:41
16		variable. Your lead compound is chosen based on a	08:57:44
17		number of variables.	08:57:48
18		So having too much flourine, in the	08:57:50
19		hypothetical, may be something you don't want to have,	08:57:52
20		or maybe having one of them in the spot you thought	08:57:54
21		was going to be good turns out to be deleterious for	08:57:58
22		other reasons.	08:58:02
23		So you can't take a myopic one variable	08:58:02
24		approach to developing a lead compound. There's	08:58:06
25		multiple facets of it, and that's why a building	08:58:10

1	block, under no circumstances, can be considered a	08:58:14
2	lead compound.	08:58:17
3	Q Under no circumstances?	08:58:26
4	A None that I'm aware of in medicinal	08:58:28
5	chemistry, where you can -- it doesn't make any sense.	08:58:31
6	It's, you know, very -- it's analogous to Legos,	08:58:35
7	really. You've got a square brick and that square	08:58:42
8	brick can be used to make a toy Ferrari or it can be	08:58:46
9	used to make a toy castle, or, you know.	08:58:51
10	My kids like to play with Legos. So, you	08:58:54
11	know, it's like saying, well, is that brick your lead	08:58:57
12	compound for how my son is going to make his Lego car.	08:59:00
13	Well, it might be how my daughter makes her Lego	08:59:05
14	princess castle, right? It's a building block.	08:59:05
15	Q Right. I mean, you're drawing a line and	08:59:09
16	you're -- you're drawing a line, it seems, and correct	08:59:14
17	me if I'm wrong, I don't want this to be inaccurate,	08:59:16
18	but you're drawing a line between oligonucleotides as	08:59:19
19	being the lead compounds, and then the building blocks	08:59:23
20	which you characterize, you know, which are reagents,	08:59:28
21	you characterize as reagents, are not lead compounds.	08:59:31
22	Is that fair --	08:59:34
23	A They are reagents. Your own expert called	08:59:36
24	them a reagent. They are reagents, that's what they	08:59:38
25	are. Your own catalog calls them reagents. They are	08:59:41

1	reagents.	08:59:44
2	Q I'm not saying that -- it's no need to be	08:59:44
3	argumentative. I'm not saying that they are --	08:59:49
4	they're not reagents.	08:59:50
5	A Okay.	08:59:51
6	Q You're testifying here, not me. So your	08:59:51
7	testimony is they are reagents.	08:59:54
8	But they're more than just reagents, though,	09:00:01
9	aren't they?	09:00:05
10	A Well, your catalog, Hongene's catalog,	09:00:05
11	Glen's catalog, Aldrich catalog, your witness,	09:00:10
12	everybody at every one of my companies calls them	09:00:13
13	reagents. They are reagents. I don't know what else	09:00:16
14	to say. I'm not being argumentative. It's just like,	09:00:19
15	okay --	09:00:23
16	Q Well, it's kind of myopic, right? I mean,	09:00:24
17	if you're just calling a class of building blocks just	09:00:27
18	reagents, you know, that seems like a label that's	09:00:30
19	being put on these building blocks, when, in fact, as	09:00:34
20	you testified earlier, these building blocks deliver	09:00:37
21	really effective ingredients to the oligonucleotide.	09:00:42
22	Would you agree with that?	09:00:46
23	A No. You don't know. Like I've seen many	09:00:47
24	cases over the past 25 years of reagents, whether	09:00:51
25	they're oligonucleotide building blocks like a	09:00:57

1 monomer, or whether it's a boronic acid for a small
2 molecule program where it's like, wow, every time we
3 incorporate this building block it works great, and
4 then they try it in a certain case, and it's like, oh,
5 dang, it doesn't work here.

6 So you have to test the whole. You can't be
7 assured that the incorporation of a particular reagent
8 is going to lead to a -- the whole molecule having the
9 properties you anticipated because it's not the lead
10 compound, it's the reagent.

11 Q But the reagent delivers -- in our example
12 of the 10 mer oligonucleotide, the reagent delivers a
13 pretty important monomer for an oligonucleotide that
14 is seeking to have higher binding affinity; wouldn't
15 you agree?

16 A No. You made up a hypothetical thing and
17 you asked me would that be one of the many candidates
18 one could look at, and I said sure. But in the
19 hypothetical, I would need to make and test and find
20 out. That's how drug discovery or any kind of
21 discovery process works.

22 I cannot be assured that the 2 fluoro or
23 whatever, the LNA, or whatever derivative -- whatever
24 building block I incorporate into an oligo is going to
25 increase the desirable properties until I make it and

1	test it.	09:02:18
2	Q But if it did end up with desirable	09:02:19
3	properties, then the core component of that	09:02:22
4	phosphoramidite that has 2-prime-fluoro --	09:02:35
5	(Court Reporter clarification.)	09:02:35
6	MR. SHORES: If -- can you read the	09:02:38
7	testimony back, please.	09:02:41
8	MR. EDWARDS: She didn't get it.	09:02:43
9	MR. SHORES: Jeremy, I'm talking about his	09:02:45
10	testimony, not mine. I'm not testifying here.	09:02:47
11	MR. EDWARDS: Okay.	09:02:50
12	(The following is read by the Court	09:03:29
13	Reporter:	09:03:29
14	"QUESTION: No. You made up a hypothetical	09:01:44
15	thing and you asked me would that be one of the many	09:01:46
16	candidates one could look at, and I said sure. But in	09:01:51
17	the hypothetical, I would need to make and test and	09:01:55
18	find out. That's how drug discovery or any kind of	09:01:58
19	discovery process works.	09:02:01
20	I cannot be assured that the 2 fluoro or	09:02:02
21	whatever, the LNA, or whatever derivative -- whatever	09:02:06
22	building block I incorporate into an oligo is going to	09:02:10
23	increase the desirable properties until I make it and	09:02:15
24	test it.")	09:02:18
25	Q But if you did incorporate the	09:03:32

1 2-prime-fluoro monomer into the oligonucleotide, and 09:03:40
2 it did increase binding affinity of the 09:03:45
3 oligonucleotide, then that 2-prime-fluoro monomer 09:03:48
4 would be pretty important to that oligonucleotide, 09:03:52
5 correct? 09:03:56

6 A If that hypothetical were true, then that 09:03:57
7 building block or that reagent would be one I would 09:04:00
8 use again. It would be an important building block, 09:04:03
9 sure, of course. 09:04:07

10 Q So we're talking about the difference -- so 09:04:08
11 we've got the reagents, we've got the phosphoramidite 09:04:10
12 reagents that have their respective protecting groups. 09:04:15

13 But within the core of that reagent is the 09:04:18
14 -- really the nucleotide -- the nucleotide that is 09:04:22
15 delivered into the oligonucleotide, correct? 09:04:27

16 A Yeah. The reagent delivers the monomer 09:04:30
17 that's incorporated into the oligonucleotide, correct. 09:04:34

18 Q So the reagent contains the monomer, right? 09:04:36

19 A Correct. 09:04:41

20 Q We've been going for about an hour. 09:05:24

21 Dr. Baran, I'll defer to you, I can keep going or if 09:05:28
22 you want to take a break. 09:05:32

23 A No, I'm fine. 09:05:34

24 Q Okay. 09:05:34

25 MR. SHORES: If we can pull up exhibit -- 09:05:39

1	for some reason I'm not seeing the -- pull up Exhibit	09:05:46
2	1003.	09:05:54
3	THE TECHNICIAN: On screen.	09:06:06
4	Q Dr. Baran, this looks familiar. This is	09:06:07
5	your opening declaration.	09:06:10
6	A Yes.	09:06:16
7	Q And if you can turn to paragraph 115, which	09:06:17
8	is page 47. Okay. Thanks. And you see the structure	09:06:22
9	there?	09:06:36
10	A Yes.	09:06:36
11	Q You've become familiar with this structure	09:06:37
12	over the course of this case, I would imagine?	09:06:40
13	A Yes, sir.	09:06:42
14	Q And what is the structure?	09:06:43
15	A It is a guanosine phosphoramidite that	09:06:44
16	contains that key 2-prime-fluoro group.	09:06:49
17	Q And is it your testimony that this is	09:06:52
18	compound X?	09:06:57
19	A Correct.	09:06:57
20	Q Okay. And you testified that compound X has	09:06:58
21	utility, right?	09:07:08
22	A Yes.	09:07:09
23	Q And you testified that -- or you agree that	09:07:10
24	compound X has a particular activity; is that right?	09:07:20
25	A Activity. It has activity in its use for	09:07:26

1	oligonucleotide synthesis. Its activity is its	09:07:33
2	ability to couple and be incorporated into an	09:07:38
3	oligonucleotide.	09:07:41
4	Q And the activity could be biological	09:07:41
5	activity once incorporated, correct?	09:07:45
6	A Once incorporated, it could endow an	09:07:47
7	oligonucleotide with better properties.	09:07:52
8	Q Could this -- I'm sorry. This is a	09:07:56
9	phosphoramidite, correct?	09:07:59
10	A Correct.	09:08:01
11	Q In your experience, has a phosphoramidite	09:08:02
12	itself ever been used as a therapeutic?	09:08:08
13	A No.	09:08:11
14	Q But you agree that the compound X can be	09:08:11
15	useful in the development of new oligonucleotide	09:08:24
16	therapeutics?	09:08:29
17	A It could be a useful building block to	09:08:31
18	explore therapeutics or diagnostics or whatever. But	09:08:35
19	it in itself is just a reagent.	09:08:41
20	Q Okay. And we see here the familiar guanine	09:08:44
21	nucleobase, correct?	09:09:08
22	A Yes.	09:09:09
23	Q And that's protected by what?	09:09:09
24	A Isobutyryl.	09:09:13
25	Q And why -- why does this need to be -- why	09:09:20

1	does -- I'm sorry. And this is at the N2 position of	09:09:26
2	-- guanine isobutyryl is attached to the N2 position	09:09:31
3	of guanine; is that correct?	09:09:35
4	A Yes.	09:09:37
5	Q Here in this compound X?	09:09:37
6	A Yes.	09:09:40
7	Q Why is that needed? Why is the protection	09:09:40
8	of the N2 position of guanine used?	09:09:44
9	A Well, in general, people protect the	09:09:50
10	nucleobases to avoid things like it dimerizing with	09:09:57
11	itself or reacting with another phosphoramidite during	09:10:03
12	the growing oligonucleotide synthesis cycle.	09:10:11
13	Q So there are certain reactivities that could	09:10:17
14	be associated with an unprotected guanine on a	09:10:21
15	phosphoramidite?	09:10:27
16	A Correct.	09:10:28
17	Q Okay. And what would happen -- so in your	09:10:29
18	opinion, you know, looking here at compound X, can	09:10:34
19	you -- if you were to use this in SPOS as a reagent,	09:10:39
20	what would happen if you didn't have isobutyryl	09:10:45
21	protecting the N2 position of guanine?	09:10:49
22	A Well, it may be that it was even difficult	09:10:53
23	to make the phosphoramidite to begin with, because if	09:10:55
24	you've got the free nitrogen and the free oxygen, you	09:10:59
25	may -- the phosphorous might attack onto the nitrogen.	09:11:04

1 You might make the phosphoramidite reagent 09:11:08
2 successfully, but then it would just decompose upon 09:11:09
3 standing by just polymerizing with itself. 09:11:13
4 You know, there could be all sorts of things 09:11:17
5 that go wrong and lower your yield. Keep in mind, 09:11:21
6 when you're growing an oligonucleotide chain, it's 09:11:24
7 important that your yields are about, you know, 98, 99 09:11:27
8 percent for a coupling step. So even a little bit of 09:11:31
9 some decomposition pathway would be really bad. 09:11:35
10 Q So -- and for purposes of compound X, you 09:11:45
11 would require there to be a protectant group at the N2 09:11:54
12 position of guanine, right? 09:11:57
13 A With phosphoramidite chemistry, yes. 09:12:00
14 Q Would that opinion change if this compound, 09:12:05
15 for example, if it was for RNA, if there was an OH 09:12:09
16 instead of an F at the 2 prime position, would you 09:12:14
17 still need a protecting group for guanine? 09:12:18
18 A Yeah, you would. You would also need a 09:12:21
19 protecting group for the 2-prime-OH. 09:12:32
20 Q Because the 2-prime-OH would be highly 09:12:35
21 reactive? 09:12:39
22 A Yeah, it would be reactive, and it would be 09:12:39
23 hard to make -- you know, that might cyclize on 09:12:42
24 itself. It would be hard to make -- reach selectively 09:12:46
25 the desired phosphoramidite, so you would need to 09:12:49

1 protect the 2-prime-OH. 09:12:53

2 Q Now, so if you had this compound X, you 09:12:57

3 know, 2-prime-fluoro, and then you had -- as compared 09:13:09

4 to the same compound, but with an OH group at the 2 09:13:15

5 prime position, would the deoxyguanosine 09:13:22

6 phosphoramidite -- or the deoxyguanosine of compound 09:13:31

7 X, would that face any issues relating to 09:13:35

8 depurination? 09:13:45

9 You know, is there a -- are you familiar 09:13:47

10 with the issue of depurination between deoxyguanosines 09:13:48

11 and regular guanosines? 09:13:54

12 A Well, you started the question with the 09:13:56

13 2-prime-OH and then you ended the question with the -- 09:14:00

14 Q I'm sorry. That's a bad question, I 09:14:03

15 apologize. It was two questions. So I'll just be 09:14:05

16 clear, you know, so I'll restate the question. And 09:14:09

17 again, I apologize for that, Dr. Baran. 09:14:11

18 Are you familiar with the issue of 09:14:15

19 depurination for deoxyguanosine? 09:14:21

20 A Yeah, it can happen. 09:14:29

21 Q And are you familiar with that depurination 09:14:33

22 issue not being as significant when you deal with 09:14:38

23 guanosine? 09:14:43

24 A You mean with free guanosine? I still don't 09:14:44

25 understand the -- you mean with -- 09:14:53

1	(Simultaneous speaking.)	09:14:53
2	Q Yeah, let me put up Exhibit 2016.	09:14:53
3	THE TECHNICIAN: Stand by, Counsel, I'm	09:15:12
4	looking for that. You said 2016?	09:15:14
5	MR. SHORES: Yes, please.	09:15:19
6	THE TECHNICIAN: That is one I'm not seeing,	09:15:44
7	I've looked through everything. Was that recently	09:15:47
8	uploaded?	09:15:50
9	MR. SHORES: Adam?	09:15:53
10	MR. NICOLAIS: Yes, I see it at the bottom.	09:15:54
11	I see it at the very bottom of the repository.	09:15:57
12	THE TECHNICIAN: I see it now. Thanks.	09:16:01
13	Give me a second to download that.	09:16:04
14	(Baran Exhibit 2016 marked for	09:16:13
15	identification.)	09:16:47
16	MR. SHORES: Are we in business here?	09:16:47
17	THE TECHNICIAN: Yes. I just had to	09:16:49
18	download it since it was recently just uploaded this	09:16:52
19	morning. Stand by.	09:16:55
20	BY MR. SHORES:	09:17:18
21	Q Okay. Dr. Baran, this is an exhibit that	09:17:18
22	ChemGene cited, Exhibit 2016, it's Iyer dated 2000.	09:17:23
23	Are you familiar with this document?	09:17:28
24	A I believe I reviewed -- I think I reviewed	09:17:30
25	this. It looks familiar.	09:17:34

1	Q	Okay. And if you would -- feel free to	09:17:37
2		familiarize yourself with it and then --	09:17:42
3	A	Okay. Where do you want to go?	09:17:46
4	Q	Okay. Cool. If you go to page 10 and	09:17:48
5		there's a heading, it says "Protection of Purine	09:17:53
6		Nucleobases: The problem of Depurination."	09:17:57
7	A	Yeah. Okay.	09:18:01
8	Q	Do you see that?	09:18:01
9		And then in the right-hand column, with the	09:18:03
10		sentence that starts with "Presence," "Presence of	09:18:07
11		the" --	09:18:11
12	A	Uh-huh.	09:18:13
13	Q	Okay. That says -- would you read that into	09:18:13
14		the record that -- those two sentences starting with	09:18:16
15		"Presence of..."	09:18:23
16	A	Okay. It says, "Presence of the 2-prime-OH	09:18:24
17		has a significant effect on the nucleoside's	09:18:29
18		susceptibility to depurination. For example,	09:18:33
19		guanosine and adenosine are more resistant to	09:18:37
20		depurination compared with deoxyadenosine and	09:18:41
21		deoxyguanosine."	09:18:45
22	Q	And so do you agree with that?	09:18:48
23	A	I mean, that's what's stated as of the 2010	09:18:54
24		-- or 2000, sorry, publication date. I agree with	09:19:01
25		that, sure.	09:19:05

1	Q	And when you're considering these -- these	09:19:10
2		compounds, if we're talking about guanosine versus	09:19:12
3		deoxyguanosine, what is your understanding as to what	09:19:21
4		the differences between those compounds are?	09:19:27
5	A	Well, the difference chemically is one has a	09:19:32
6		2-prime-OH and one does not. And as a corollary to	09:19:37
7		that, one has to be careful to minimize or attenuate	09:19:40
8		exposure to acidic conditions which are known to	09:19:46
9		rapidly depurinate those types of systems.	09:19:49
10	Q	And then those two compounds, the guanosine	09:19:54
11		and deoxyguanosine compounds react differently under	09:19:59
12		those conditions, correct?	09:20:07
13	A	Yes.	09:20:08
14	Q	Okay.	09:20:09
15	MR. SHORES:	Okay. We can take this one	09:20:39
16		down.	09:20:42
17	Q	All right. So if we go back to the compound	09:20:59
18		X, which I guess is Exhibit 1003, at paragraph 115.	09:21:03
19		And we're back there, Dr. Baran, do you see	09:21:21
20		that compound on paragraph 115?	09:21:24
21	A	Yes, sir.	09:21:26
22	Q	And that's compound X, right?	09:21:27
23	A	Yes.	09:21:29
24	Q	Before you selected compound X in your	09:21:30
25		obviousness analysis in this case, were you aware of	09:21:40

1	the degradation issues associated with using it?	09:21:46
2	A There's a potential for degradation in many	09:21:51
3	types of monomers. So that wasn't part of the -- the	09:21:57
4	analysis. The analysis is basically if a medicinal	09:22:05
5	chemist needs to incorporate a 2-prime-fluoro	09:22:09
6	guanosine structure, they would go to a database like	09:22:13
7	SciFinder, search for that monomer structure, locate	09:22:19
8	it in this patent, they would be enabled in terms of	09:22:23
9	the synthesis of the compound by this patent and they	09:22:29
10	would proceed forward. That would be the extent to	09:22:32
11	which they would use this literature.	09:22:34
12	Q I was asking if you were aware of the --	09:22:39
13	before you selected this compound to use in your	09:22:43
14	opinions relating to obviousness, were you aware of	09:22:49
15	the degradation issues associated with using it?	09:22:55
16	A I'm aware of the degradation issues	09:22:58
17	associated with -- in general, it being something to	09:23:01
18	look out for.	09:23:05
19	Q But were you aware of the degradation issues	09:23:07
20	associated with -- with it when you were -- wrote your	09:23:12
21	original declaration in January of 2023?	09:23:16
22	A I'm not aware that there are any documented	09:23:19
23	examples of degradation issues that are insurmountable	09:23:24
24	with this compound.	09:23:29
25	Q That's not what I asked, respectfully.	09:23:30

1	It's a simple question of whether you were	09:23:32
2	aware of the degradation issues relating to using	09:23:35
3	compound X when you submitted your January 2023	09:23:41
4	declaration?	09:23:46
5	MR. EDWARDS: Object to form.	09:23:47
6	A As I said, I'm aware that it has to be	09:23:50
7	something to look out for in all cases. But as far as	09:23:53
8	it being a specific problem associated with this	09:23:56
9	compound, no.	09:23:59
10	Q No, you weren't aware at that time when you	09:24:02
11	submitted your January 2023 declaration?	09:24:05
12	MR. EDWARDS: Object to form. Vague. And	09:24:07
13	mischaracterizing testimony.	09:24:11
14	MR. SHORES: I'm just trying to get an	09:24:12
15	answer to my question here.	09:24:13
16	MR. EDWARDS: And I'm objecting.	09:24:15
17	MR. SHORES: I understand.	09:24:16
18	A I mean, I don't know what else to add to	09:24:18
19	what I said.	09:24:21
20	Q Simple answer, were you aware of the	09:24:24
21	degradation issues relating to using compound X when	09:24:29
22	you submitted your January 2023 declaration?	09:24:38
23	MR. EDWARDS: Object to form. Vague.	09:24:41
24	Mischaracterizing testimony. Asked and answered.	09:24:43
25	MR. SHORES: Not asked and answered.	09:24:48

1	A	Well, I was aware in general that you always	09:24:51
2		have to be on the lookout for degradation issues. And	09:24:55
3		for this compound in particular, I wasn't aware of any	09:24:59
4		specific literature that pointed to this compound	09:25:02
5		being problematic for specific degradation.	09:25:05
6	MR. SHORES:	Okay. This is a good stopping	09:25:14
7		point for a break. You guys want to take 10 minutes?	09:25:15
8		Is that okay with you, Dr. Baran?	09:25:19
9	THE WITNESS:	Whatever you say, you're the	09:25:22
10		boss. So 6:35 a.m. or 9:35 a.m. for you?	09:25:23
11	MR. SHORES:	Correct.	09:25:28
12	THE WITNESS:	Okay. Thanks.	09:25:30
13	THE VIDEOGRAPHER:	We are going off of the	09:25:34
14		record at 9:25 a.m.	09:25:36
15		(Recess 9:25 a.m. - 9:37 a.m.)	09:25:39
16	THE VIDEOGRAPHER:	We are going back on the	09:37:10
17		record at 9:37 a.m.	09:37:12
18	MR. SHORES:	Hi, Dr. Baran. Actually, could	09:37:18
19		we pull up Exhibit 1018, please.	09:37:20
20	THE TECHNICIAN:	Stand by.	09:37:32
21	MR. SHORES:	I meant to say welcome back,	09:37:34
22		Dr. Baran.	09:37:37
23	THE WITNESS:	Thanks.	09:37:40
24		(Baran Exhibit 1018 marked for	09:37:53
25		identification.)	09:37:56

1	Q	Dr. Baran, you've seen this exhibit before?	09:37:56
2		This is Exhibit 1018.	09:37:59
3	A	Yes.	09:38:01
4	Q	And what is this document?	09:38:01
5	A	This is the Pitsch paper that we talk about	09:38:03
6		a lot in this case.	09:38:07
7	Q	Okay. So you agree that in this paper	09:38:17
8		Pitsch studied the synthesis of RNA-based	09:38:24
9		oligonucleotides, right?	09:38:33
10	A	Yes.	09:38:40
11	Q	And then if you go to page 2, which is page	09:38:40
12		3774 of the article, and if you look at the last full	09:38:48
13		paragraph, bottom, Pitsch describes -- well, would you	09:38:59
14		mind reading that last paragraph in the record,	09:39:11
15		please?	09:39:13
16	A	Sure. "We now describe in detail the	09:39:14
17		preparation of 2 prime-O-[[triisopropylsilyl)	09:39:16
18		oxy)methyl}-protected(=2 prime-O-tom-protected)	09:39:37
19		phosphoramidites of the four canonical ribonucleosides	09:39:46
20		and summarize all necessary information required for	09:39:52
21		their application in the routine synthesis of	09:39:55
22		oligoribonucleotides. Preliminary results obtained	09:39:58
23		with these novel RNA building blocks were published	09:40:03
24		previously."	09:40:08
25	Q	So you agree this paper describes the	09:40:09

1	synthesis of oligonucleotides utilizing, quote, "novel	09:40:13
2	RNA building blocks," right?	09:40:19
3	A Yes.	09:40:21
4	Q And in your opinion, what was novel about	09:40:30
5	the building blocks, the RNA building blocks in	09:40:36
6	Pitsch?	09:40:40
7	A Well, there were a number of features that	09:40:41
8	were novel. The use of the 2 prime-tom, the	09:40:43
9	disclosure of the acetyl protecting group as a	09:40:49
10	universal nucleobase protection method for rapid	09:40:54
11	deprotection. Those are two of the -- some of the	09:41:00
12	novel aspects.	09:41:04
13	Q Okay. So -- I'm sorry. So the first novel	09:41:06
14	aspect was the tom group?	09:41:15
15	A The tom-protected phosphoramidites, their	09:41:18
16	synthesis.	09:41:22
17	Q And what was, in your opinion, you know,	09:41:23
18	based on reading the literature here that the Pitsch	09:41:27
19	-- this Pitsch paper, Exhibit 1018, what was novel	09:41:31
20	about the tom-2-prime protecting group?	09:41:36
21	A Its utility in RNA oligonucleotide	09:41:43
22	synthesis, which is disclosed here, that -- the	09:41:53
23	demonstration that that group is advantageous in this	09:41:56
24	context.	09:42:03
25	Q Would you call that the main innovation?	09:42:05

1	Would you say it's the sort of headliner, for lack of	09:42:10
2	a better term?	09:42:13
3	A I'm not sure if it's the headliner because	09:42:14
4	you need all the pieces to make it work. And I think	09:42:19
5	one of those key pieces to, you know, get this	09:42:22
6	chemistry robust was also the use of the acetyl	09:42:25
7	nucleobase protection, which can be used in DNA or	09:42:34
8	RNA.	09:42:38
9	Q So if we look at, you know, go to page 6,	09:42:38
10	which is 3778, and then you've quoted this a number of	09:42:47
11	times, but if you wouldn't mind reading the sentence	09:43:00
12	that starts with "These values indicated..."	09:43:04
13	A [As read]: "These values indicated that	09:43:08
14	complete base-deprotection of oligonucleotide	09:43:12
15	sequences can be achieved within 1 hour (equal to 15	09:43:15
16	half-lives for the acetylated guanosine residues) and	09:43:20
17	demonstrated that the Ac group, in combination with	09:43:26
18	methylamine is indeed suited for a labile universal	09:43:30
19	nucleobase protection."	09:43:36
20	Q And what is your interpretation of	09:43:39
21	"universal" here?	09:43:42
22	A Meaning it can be used on virtually any	09:43:44
23	nucleobase, regardless of the sugar substitution or	09:43:51
24	the type of nucleobase.	09:43:55
25	Q So where in Pitsch does it say that?	09:44:00

1	A	That's -- well, you asked me what I	09:44:04
2		interpreted universal to mean, and that's what I	09:44:09
3		interpreted universal to mean.	09:44:12
4	Q	So that's based on -- that's not based on	09:44:14
5		any statement that's made in Pitsch other than that	09:44:18
6		one sentence, correct?	09:44:22
7	A	Well, it's based on the Merriam-Webster	09:44:24
8		definition of what universal means.	09:44:27
9	Q	So your testimony is that this Pitsch paper	09:44:31
10		teaches using -- that acetyl can be used for any	09:44:38
11		nucleoside, to protect any base of any nucleoside?	09:44:45
12	A	That it's a great option for doing that,	09:44:49
13		that's what universal implies here.	09:44:51
14	Q	Well, what is your -- I'm asking what	09:44:54
15		your -- if that's your interpretation.	09:44:58
16	A	Yeah, that's my interpretation.	09:45:01
17	Q	And that's not based on anything in this	09:45:06
18		paper other than that one sentence, correct?	09:45:09
19	MR. EDWARDS:	Object to form. Asked and	09:45:11
20		answered.	09:45:15
21	A	Well, no. It's based on the data presented.	09:45:15
22		They wouldn't be able to make such a broad claim	09:45:18
23		without supportive data, which they have.	09:45:21
24	Q	But that data didn't include data relating	09:45:23
25		to 2 prime-fluoro or 2 prime-deoxyguanosine, correct?	09:45:26

1	A	That's correct. But a person of skill in	09:45:34
2		the art, anyone that would read this paper would not	09:45:39
3		assume that the -- that a small substitution like a	09:45:43
4		flourine would take away from the universality of the	09:45:49
5		Ac protecting group.	09:45:55
6	Q	In fact, the data presented in Pitsch only	09:45:57
7		relates to these novel 2-prime-tom RNA nucleosides,	09:46:01
8		correct?	09:46:09
9	A	Yes.	09:46:09
10	Q	If you can turn to page 14, which is 3786 of	09:46:10
11		the article, and in the paragraph that starts with	09:46:30
12		"The separation..." So it's a little bit farther	09:46:51
13		down.	09:46:55
14		In the sentence that starts with	09:46:59
15		"Furthermore," I'll read this one into the record this	09:47:01
16		time to give you a break here.	09:47:04
17		This article -- this section of Exhibit 1018	09:47:07
18		on page 14 says, "Furthermore, due to the stability of	09:47:10
19		the 2 prime-O-tom group, a variety of nucleobase and	09:47:15
20		sugar manipulations can be carried out after its	09:47:20
21		introduction. Therefore, we were able to carry out	09:47:24
22		short and convergent syntheses of ribonucleoside	09:47:27
23		analogues and of building blocks with different	09:47:33
24		nucleobase-protecting groups."	09:47:37
25		Did I read that correctly?	09:47:39

1	A	Yes.	09:47:42
2	Q	So doesn't this indicate that other	09:47:42
3		nucleobase-protecting groups were used but not acetyl?	09:47:44
4	A	I mean, it implies here that the issue of	09:47:54
5		the 2 tom -- 2 prime-tom protecting group is a good	09:48:00
6		protecting group for RNA and that can be employed in	09:48:04
7		concert with a variety of nucleobase-protecting	09:48:10
8		groups.	09:48:16
9	Q	And it says "due to the stability of the 2	09:48:16
10		prime-tom group," what do you interpret that as	09:48:20
11		meaning?	09:48:22
12	A	That it doesn't essentially fall off during,	09:48:23
13		let's say, DMT deprotection conditions.	09:48:27
14	Q	Doesn't that indicate that -- withdraw the	09:48:33
15		question.	09:49:06
16		Before you testified that you interpreted	09:49:07
17		this document as acetyl being one of the novel aspects	09:49:11
18		-- using acetyl as a nucleobase-protecting group to be	09:49:18
19		a novel aspect of Pitsch, correct?	09:49:22
20	A	Yes.	09:49:27
21	Q	What is that based on?	09:49:33
22	A	It's based on the data presented in the	09:49:36
23		paper, which was quite instructive, and it's one of	09:49:40
24		the very nice examples out there, which is why they	09:49:47
25		highlight it, of the utility of the acetyl-protecting	09:49:51

1	group.	09:49:55
2	Q You're not aware of any other literature	09:49:55
3	that used acetyl to protect guanine on a guanine-based	09:50:00
4	nucleoside?	09:50:10
5	A I think there are examples out there, I may	09:50:11
6	have referenced them. But what's nice about the	09:50:14
7	Pitsch paper is how they call it out specifically and	09:50:19
8	they point to its, you know, utility in a really	09:50:22
9	complicated context. And that would be a very	09:50:28
10	strong -- this paper would be a very strong precedent	09:50:30
11	for a motivational feature for a practitioner seeking	09:50:35
12	to reduce deprotection times.	09:50:40
13	Q I mean, it's not novel, right? Is that what	09:50:43
14	you're saying?	09:50:45
15	You're saying that you're familiar with some	09:50:47
16	literature that taught the same thing. So it's not	09:50:50
17	novel, right? I mean, is that fair to say?	09:50:53
18	A Well, it's novel in this context.	09:50:55
19	Q In the context of 2 prime-O-tom?	09:50:59
20	A Yeah, in general, a more complicated -- like	09:51:03
21	a more complicated oligonucleotide and then making	09:51:07
22	these sequences and then doing it and having this	09:51:11
23	really extensive and exhaustive experiment data.	09:51:14
24	So this is a key reference because a person	09:51:21
25	of skill in the art would look at this really	09:51:24

1	well-documented, beautifully enabled publication as	09:51:27
2	very strong reason to want to employ an acetyl versus	09:51:30
3	maybe other literature that didn't as explicitly point	09:51:36
4	out the advantageous features of an acetyl.	09:51:40
5	Q But all of that experimental data and all of	09:51:44
6	that enabled -- beautifully enabled subject matter	09:51:50
7	that's in this paper only relates to 2 prime-tom	09:51:55
8	nucleosides, right?	09:52:02
9	A Why else --	09:52:08
10	MR. EDWARDS: Object to form.	09:52:08
11	Sorry, sorry, Dr. Baran. I was slow to	09:52:10
12	unmute. I just wanted to object to form. Please try	09:52:13
13	to answer.	09:52:21
14	A While that is true, a POSA looking at this	09:52:21
15	would be quite compelled to employ it in their own	09:52:24
16	work, because the tom is a rather complicated	09:52:29
17	nucleobase, the 2 prime-tom protection is rather	09:52:34
18	complicated. So the POSA would look at this and say,	09:52:38
19	wow, if it works in this complicated context, then my	09:52:42
20	context is going to work as well.	09:52:45
21	And that's supported by two things. One,	09:52:47
22	the experimental data, which shows and implies that	09:52:51
23	this is a really useful and universal nucleobase	09:52:54
24	protecting group; and number two, the -- the fact that	09:52:59
25	they actually made these long sequences and	09:53:04

1	demonstrated it and have really compelling data.	09:53:06
2	It's not like a very short publication where	09:53:11
3	the experimental section is kind of brief or something	09:53:14
4	is mentioned in a footnote. It's beautifully	09:53:19
5	described and enabled in a really complicated	09:53:23
6	scenario.	09:53:26
7	The other thing that should be mentioned is	09:53:27
8	that the substituents on the sugar ring are very far	09:53:31
9	away from the nucleobase, and in general, do not have	09:53:38
10	a huge effect on the deprotection rate of the	09:53:47
11	nucleobase because it's very far from the sugar. So a	09:53:51
12	POSA would look at this and they would say whatever	09:53:55
13	substituent I have on my sugar is not really -- is not	09:53:59
14	really going to be a problem because of what the work	09:54:06
15	described herein.	09:54:11
16	Q And you would agree that using acetyl as a	09:54:12
17	protecting group was well known in 2009, correct?	09:54:21
18	A Yes.	09:54:27
19	Q And it goes back to Khorana, right?	09:54:28
20	A Well, invoking that old literature, you	09:54:34
21	know, the problem is science evolves, and if you go	09:54:38
22	back far enough in the literature, you can be	09:54:44
23	convinced that the earth is flat.	09:54:49
24	So in general, the POSA is going to try to	09:54:51
25	find the most up-to-date, recent, and well-described	09:54:54

1 experimental details for the modern era. So while 09:54:59
2 Khorana is really useful literature in the classroom, 09:55:04
3 that literature is for really a different system all 09:55:07
4 together, phosphate ester-type methods, not 09:55:12
5 phosphoramidite. 09:55:15

6 So if you put a 1960 Khorana paper next to 09:55:16
7 this paper and ask the POSA which one do you want to 09:55:22
8 use as your guiding reference, no one would pick the 09:55:27
9 Khorana reference for anything other than historical 09:55:30
10 understanding of how the field progressed. 09:55:33

11 MR. SHORES: You can take the exhibit down. 09:55:47

12 Q So you see no -- sitting here today -- or as 09:55:54
13 of 2009, you didn't -- your testimony is a POSA would 09:55:58
14 not have viewed Khorana as useful at all other than in 09:56:03
15 a historical context? 09:56:10

16 A As historical context; that having the 09:56:11
17 Khorana paper with an acetyl group with a completely 09:56:14
18 different type of coupling methodology -- you know, in 09:56:20
19 general, you're not -- a POSA is not going to use a 09:56:23
20 1960s paper as a guide for their experimental 09:56:27
21 conditions. They're going to look for the most 09:56:31
22 up-to-date and well-documented literature from the 09:56:34
23 modern era to base their experimental design. 09:56:36

24 Q Right. And so all of the, you know, 09:56:41
25 scientists that follow Khorana into the 09:56:44

1 phosphoramidite era, this phos era up until 2009 and 09:56:51
2 after that that cited to Khorana, they are just citing 09:56:58
3 to Khorana for historical context and not for 09:57:01
4 scientific reasons? 09:57:05

5 A Well, that question is really broad. I 09:57:06
6 mean, there's probably thousands of citations to 09:57:08
7 Khorana for a variety of different reasons. So if you 09:57:11
8 want to point to a specific paper, we can look at it 09:57:16
9 and I can tell you why they likely cited it. 09:57:19

10 Q You didn't identify any papers after Pitsch 09:57:23
11 that used acetyl with guanine on a guanine-based 09:57:27
12 nucleoside, though, correct? 09:57:33

13 A I didn't need to look for more than Pitsch. 09:57:38

14 Q But you didn't -- you didn't identify any 09:57:42
15 other literature, correct? 09:57:44

16 A After we -- after I identified -- after I 09:57:47
17 identified Pitsch, I felt that was compelling enough 09:57:53
18 to base this argument. 09:57:56

19 Q But you testified -- you testified earlier 09:58:05
20 that isobutyryl is a known standard protecting group 09:58:10
21 for guanosine, correct? 09:58:21

22 A So is benzoyl. 09:58:27

23 Q And you didn't identify any papers at all 09:58:29
24 that used acetyl to protect deoxyguanosine, right? 09:58:34

25 A I don't recall if I looked. I don't recall 09:58:42

1	if I needed to look for that.	09:58:45
2	Q The compounds are -- at issue are	09:58:49
3	deoxyguanosine compounds, correct?	09:58:53
4	A Deoxy and 2 fluoro.	09:58:55
5	Q And that's what Khorana studied, right?	09:58:58
6	A Khorana studied all of them, but I don't	09:59:01
7	think he was using phosphoramidites to do that.	09:59:05
8	Q But you would agree that Khorana taught away	09:59:08
9	from using acetyl in connection with his	09:59:13
10	experimentations?	09:59:18
11	A Well, his experimentations are not relevant	09:59:18
12	because he was not doing phosphoramidite chemistry,	09:59:22
13	and he was using equipment, reagents, and know-how	09:59:26
14	from 50 years before the POSA date. So a lot changed	09:59:29
15	in 50 years.	09:59:38
16	Q But in the context of his study and	09:59:48
17	phosphodiester chemistry, you would agree that he	09:59:51
18	taught away from using acetyl, right?	09:59:55
19	A Yeah, in a completely different context. I	09:59:59
20	think the preferred protecting group for that	10:00:04
21	completely different manifold for making	10:00:07
22	oligonucleotides was other types of acetyl protecting	10:00:10
23	groups. But, again, that literature is not something	10:00:15
24	a POSA would be -- would be inspired by because it's	10:00:18
25	not phosphoramidite.	10:00:23

1	Q	You're familiar with the Schulhof reference,	10:00:24
2		Dr. Baran?	10:00:46
3	A	You can pull it up.	10:00:46
4	Q	Okay, if you want to.	10:00:50
5	A	Sure.	10:00:51
6	Q	That would be Exhibit 2013.	10:00:52
7		(Baran Exhibit 2013 marked for	10:00:58
8		identification.)	10:01:28
9	Q	You're familiar with this document,	10:01:28
10		Dr. Baran?	10:01:30
11	A	I believe so. Yeah, mm-hmm.	10:01:31
12	Q	Okay. And it's your understanding that the	10:01:52
13		Schulhof features the phenoxyacetyl as an alternative	10:01:57
14		to isobutyryl, right?	10:02:04
15	A	Yes.	10:02:07
16	Q	But Schulhof doesn't teach using acetyl,	10:02:07
17		correct?	10:02:12
18	A	I don't -- I don't think so. No, I don't	10:02:12
19		think so.	10:02:33
20	Q	What's the date of this reference here?	10:02:33
21	A	1987, I believe.	10:02:49
22	Q	So this is in the phosphoramidite era?	10:02:50
23	A	This is sort of when the phosphoramidite era	10:02:53
24		started really ramping up, in the '80s is when that	10:02:56
25		happened.	10:03:02

1	MR. SHORES: Okay. You can take that down,	10:03:18
2	Jack.	10:03:21
3	If we can go back to Exhibit 1018, please.	10:03:49
4	1018, Jack.	10:04:11
5	THE TECHNICIAN: I'm sorry, I'm having an	10:04:13
6	issue --	10:04:15
7	MR. SHORES: That's all right. I just	10:04:19
8	didn't know if you heard me, that's all.	10:04:20
9	THE TECHNICIAN: Stand by.	10:04:20
10	BY MR. SHORES:	10:04:20
11	Q Okay. If you can go to the figure where	10:04:24
12	compound 20 is shown. We both probably have it	10:04:27
13	memorized, I guess. I don't yet.	10:04:32
14	THE TECHNICIAN: Let me switch that for you.	10:04:36
15	Stand by. Okay.	10:04:38
16	BY MR. SHORES:	10:04:48
17	Q Okay. So looking at compound 20, which I	10:04:48
18	guess is the compound on the lower right-hand corner?	10:04:55
19	A Yeah.	10:04:59
20	Q Do you agree with that?	10:04:59
21	A Mm-hmm.	10:05:01
22	Q And so if you were to switch the OH and tom	10:05:02
23	group, which is at the 2 prime position -- you agree	10:05:09
24	that OH and tom is at 2 prime?	10:05:13
25	A Yes.	10:05:15

1	Q	If you were to switch that --	10:05:15
2	A	Sorry. Sorry, I'm not sure I agree with	10:05:24
3		that.	10:05:26
4	Q	Okay. Tell me what, yeah, like that --	10:05:26
5	A	The tom is at 2 prime, the phosphoramidite	10:05:26
6		is at 3 prime.	10:05:30
7	Q	Okay. So the compound in the lower	10:05:32
8		right-hand corner -- and what figure is this? Scheme	10:05:34
9		1 I should say.	10:05:39
10		So the compound in the lower right-hand	10:05:40
11		corner of Scheme 1 --	10:05:42
12	A	Yes.	10:05:44
13	Q	-- what is that compound?	10:05:44
14	A	That is 2 prime-tom. If it's compound 20	10:05:46
15		you're talking about, the base identification is	10:05:50
16		guanosine. It's got acetyl at the N2 position. And	10:05:52
17		at the 3 prime position is a phosphoramidite, and at	10:05:57
18		the 5 prime is a DMT.	10:06:02
19	Q	Okay. So if you were to switch the 2	10:06:04
20		prime-tom -- and it's really protecting OH, right?	10:06:08
21		It's protecting O --	10:06:11
22	A	The tom is the protecting the 2 prime OH,	10:06:13
23		correct.	10:06:16
24	Q	Right. So if you were to replace that	10:06:17
25		with -- with fluoro, you would agree that that	10:06:19

1 compound would be less soluble in organic solvents? 10:06:26

2 A I'm not sure. 10:06:32

3 Q So you don't know one way or the other? 10:06:37

4 A No. I can make a guess. But if I were a 10:06:40

5 POSA, I would not be concerned about the solubility 10:06:46

6 because I'm going to be using something like 10:06:51

7 acetonitrile, NMP. So I wouldn't a priori look at 10:06:55

8 that compound and say, oh, that's going -- that's 10:06:57

9 going to be a problem for a synthesizer in terms of 10:07:00

10 getting it into a stock solution. So no red flags 10:07:04

11 from my vantage point. 10:07:07

12 Q Right, you're saying no red flags. But I 10:07:09

13 was asking whether you would expect -- or whether a 10:07:12

14 POSA would expect that by switching the tom-OH, you 10:07:15

15 know, substituent and inserting fluoro, whether the 10:07:20

16 compound with fluoro would be less soluble in organic 10:07:27

17 solvents? 10:07:31

18 A I'm not sure that they would ever even think 10:07:34

19 about that. 10:07:38

20 Q Well, I'm asking it. If they were to think 10:07:40

21 about that, if someone were to pose that question to a 10:07:44

22 POSA, if you switched the 2-prime-OH-tom, switched 10:07:48

23 that -- switched in fluoro, switched out 10:07:53

24 2-prime-OH-tom, whether the resulting compound with 10:07:58

25 the 2-prime-fluoro would be less soluble in organic 10:08:00

1	solvents?	10:08:05
2	A I think a POSA would probably say that the	10:08:06
3	compound 20 depicted here is more lipophilic than the	10:08:09
4	compound with the fluorine. But in terms of relative	10:08:15
5	solubility, I'm not sure it would be easy to predict	10:08:19
6	one way or the other.	10:08:24
7	Perhaps some people would say, oh, maybe it	10:08:26
8	will be slightly less soluble. Some people would say	10:08:28
9	it's probably going to be the same for the purposes of	10:08:32
10	making a stock solution for an oligo synthesizer.	10:08:36
11	MR. SHORES: If we can pull up Exhibit 1029,	10:08:54
12	please.	10:08:58
13	THE TECHNICIAN: Stand by.	10:09:03
14	(Baran Exhibit 1029 marked for	10:09:17
15	identification.)	10:09:40
16	Q Have you seen this document, Doctor?	10:09:40
17	A Looks familiar. I would have to reacquaint	10:09:50
18	myself with it. It looks familiar. Is there a	10:09:53
19	specific spot you want me to go to?	10:10:02
20	Q Yes. If you go to page 3 and Scheme 3, and	10:10:09
21	then the compound in the lower right-hand corner.	10:10:18
22	And a similar question as before, if you	10:10:31
23	were to -- so what's at the 2 prime position?	10:10:36
24	A This time it's an OTBDMS group.	10:10:40
25	Q Right. And if you were to switch the OTBDMS	10:10:44

1	group with fluoro, would you consider the compound	10:10:51
2	with fluoro to be less soluble in organic solvents?	10:10:56
3	A My answer would be the same. I think you	10:11:02
4	would have a handful of people that would say there	10:11:05
5	would be very little difference in solubility. Some	10:11:07
6	people may say slightly less soluble.	10:11:11
7	But the point of -- the POSA would only look	10:11:14
8	at solubility insofar as it matters for making a stock	10:11:19
9	solution for insulation on an oligonucleotide	10:11:24
10	synthesizing machine. The POSA doesn't evaluate	10:11:30
11	reagents and say, oh, let me predict what the molarity	10:11:35
12	concentration of a supersaturated solution is going to	10:11:41
13	be. They look at it and they say, yeah, it's going to	10:11:44
14	be soluble; or no, that thing is going to be	10:11:47
15	intractable, we need to solubilize it somehow. It's	10:11:49
16	sort of a binary question that they ask in their head.	10:11:53
17	MR. SHORES: Can we go to Exhibit 1038,	10:11:59
18	please.	10:12:04
19	THE TECHNICIAN: Stand by.	10:12:05
20	(Baran Exhibit 1038 marked for	10:12:06
21	identification.)	10:12:39
22	MR. SHORES: Actually, can we go to Exhibit	10:12:39
23	1033. We want to come back to this, but 1033, which	10:12:41
24	is Dr. Baran's second declaration.	10:12:46
25	THE TECHNICIAN: Stand by.	10:12:49

1	MR. SHORES: Paragraph 55.	10:12:51
2	Q Do you see that paragraph, 55, Dr. Baran?	10:13:33
3	A Yes.	10:13:35
4	Q Can you read the sentence into the record	10:13:36
5	that says "This is illustrated..."	10:13:48
6	A "This is illustrated, for example, by Zhu	10:13:51
7	(2003), et al., which shows that under substantially	10:13:57
8	the same reaction conditions, there were little or no	10:14:01
9	differences in silylation time and benzylation time	10:14:04
10	of various nucleosides, regardless of which group was	10:14:09
11	attached to the 2 prime position of the sugar ring."	10:14:12
12	MR. SHORES: Now if we can go to Exhibit	10:14:18
13	1038, and go to Table 1.	10:14:20
14	Q And then in looking at this chart, what is	10:14:30
15	the silylation time of guanosine which is row 3?	10:14:34
16	A Silylation time, .5 hours.	10:14:39
17	Q And then what about 2 prime-deoxyguanosine	10:14:44
18	monohydrate in row 10?	10:14:49
19	A 1.5 hours.	10:14:51
20	Q Isn't that -- isn't the silylation time of	10:14:53
21	2 prime-deoxyguanosine monohydrate three times that of	10:14:58
22	guanosine?	10:15:04
23	A That is correct. But it's the guanosine	10:15:14
24	monohydrate versus the guanosine, so -- but half an	10:15:16
25	hour versus one-half hours is, for a monomer, it's --	10:15:23

1	that's not a -- not a big difference in time for an	10:15:30
2	organic chemist.	10:15:34
3	Q And then similarly, with respect to	10:15:35
4	benzoylation time for guanosine, that is two hours,	10:15:37
5	correct?	10:15:43
6	A Yes.	10:15:44
7	Q And then the benzoylation time for	10:15:45
8	2 prime-deoxyguanosine monohydrate is six hours,	10:15:50
9	correct?	10:15:56
10	A Yes.	10:15:56
11	Q So then the benzoylation time for	10:15:56
12	2 prime-deoxyguanosine monohydrate is three times that	10:16:00
13	of guanosine according to this table, correct?	10:16:02
14	A Yes.	10:16:04
15	Q Thank you.	10:16:05
16	MR. SHORES: You can take this one down,	10:16:15
17	please.	10:16:17
18	Q So in terms of the, you know, degradation	10:16:37
19	issue, so if we go to your declaration Exhibit 1033,	10:16:42
20	at paragraph -- it's paragraphs 57 to 61.	10:16:48
21	So I just want to be clear as to what your	10:17:06
22	testimony is relating to the degradation. Are you	10:17:10
23	saying that there was a degradation issue but it had	10:17:16
24	been resolved?	10:17:21
25	Like, can you please describe your views on	10:17:22

1 the degradation issues relating to 10:17:28
2 2 prime-fluoro-2-prime-deoxyribonucleotides? 10:17:31
3 A Well, I think that the -- ChemGenes' 10:17:37
4 argument of a degradation issue is a strawman 10:17:40
5 argument. It's an imaginary problem which is not 10:17:44
6 documented by anyone, some sort of conference 10:17:48
7 proceeding that we don't know what it is. And the 10:17:53
8 Kawasaki paper that is pointed to by ChemGenes in -- 10:17:55
9 within contains the answer to the problem. 10:18:00
10 So it's a problem which is, you know, to 10:18:04
11 some degree, undocumented. But if it were to occur, 10:18:10
12 there are solutions that are contained within 10:18:14
13 ChemGenes' own documents that they provided. 10:18:18
14 And furthermore, if they were persistent 10:18:21
15 problems to the POSA, they would be easily rectified 10:18:26
16 by either change in the deprotection conditions or 10:18:30
17 switching over to a more labile nucleobase-protecting 10:18:33
18 group. 10:18:38
19 Q And what was the -- so are you saying -- are 10:18:38
20 you saying that the literature does not show there was 10:18:42
21 even -- there was any problem at all? 10:18:44
22 A Well, the literature that pointed to the 10:18:46
23 problem also solved the problem. 10:18:48
24 Q Okay. So when you say "the problem," then 10:18:50
25 you're saying that there was a problem; it's just 10:18:53

1 there was a solution offered. 10:18:57

2 A There was one solution offered in the very 10:18:59
3 paper they cite as being problematic. 10:19:04

4 Q Right. But in order for there to be a 10:19:07
5 solution, there has got to be a problem in the first 10:19:10
6 place. So I'm just looking to see if you agree that 10:19:13
7 there was a problem in the first place. 10:19:16

8 A Well, I mean, there was a problem carrying 10:19:17
9 goods before the wheel was invented, too. So should 10:19:20
10 we list transportation as a problem, too? 10:19:24

11 I mean, so it's like -- it's a fallacious 10:19:28
12 argument, because it's like, yeah, there's a problem, 10:19:30
13 it existed in history, and there are many solutions 10:19:34
14 that were available to the POSA at the time. So that 10:19:37
15 it's not even clear that they would have encountered 10:19:41
16 this problem, nor has ChemGenes provided any documents 10:19:44
17 that show that this was a pressing problem. 10:19:48

18 I'm not aware of it. Maybe you can provide 10:19:50
19 something. 10:19:53

20 Q Well, doesn't Sinha identify the problem of 10:19:54
21 depyrimidination? 10:20:00

22 A Not really. He points to a book chapter in 10:20:03
23 2013, which is not in the POSA time frame, and a 10:20:07
24 conference proceeding which nobody has access to. 10:20:10

25 So if a POSA were to look in the literature, 10:20:15

1	they wouldn't find whatever it is Sinha is referring	10:20:18
2	to. They would find maybe Kawasaki's reference and	10:20:21
3	they would see, oh, here is how I solve it.	10:20:26
4	Q So you're saying that Kawasaki did identify	10:20:29
5	the degradation problem?	10:20:33
6	A They identified a problem which is easily	10:20:35
7	rectified by simply changing their deprotection	10:20:37
8	conditions.	10:20:40
9	Q So the testimony is -- your testimony is	10:20:41
10	there was a problem, correct, relating to degradation,	10:20:42
11	correct?	10:20:49
12	A Kawasaki claimed there was a problem, I	10:20:49
13	don't know when that date that was -- whatever the	10:20:55
14	date of that publication, in the '80s or '90s. I'm	10:20:56
15	not sure. Let's see in here, let's see when does	10:20:59
16	Kawasaki --	10:21:04
17	Q You can pull up Exhibit 2025, and in your	10:21:06
18	dec it would be somewhere in 57 to 61, but we can pull	10:21:09
19	up the Kawasaki and make it easier.	10:21:14
20	(Baran Exhibit 2025 marked for	10:21:14
21	identification.)	10:21:14
22	Q And then I guess if we go to page 833. I	10:21:33
23	guess we can go back up to the top, just to get the	10:21:53
24	date in here. So what is the date of this paper,	10:21:56
25	Dr. Baran?	10:22:02

1	A	1993.	10:22:02
2	Q	And this was well into the SPOS era?	10:22:05
3	A	Oh, yeah.	10:22:10
4	Q	So if we can go to page 833 of the article	10:22:12
5		of Exhibit 2025.	10:22:17
6		Do you see the paragraph that starts with	10:22:29
7		"Synthesis of 2 prime-deoxy-2 prime-fluoro-containing	10:22:33
8		oligonucleotides"?	10:22:37
9	A	Yes.	10:22:38
10	Q	And I'll read that into the record this	10:22:39
11		time. "The 2 prime-deoxy-2-prime-fluoro-modified	10:22:43
12		oligonucleotides were prepared in moderate yields. As	10:22:50
13		it has been reported that the	10:22:54
14		2 prime-deoxy-2-prime-fluoro pyrimidines are	10:22:56
15		susceptible to elimination of fluoride under basic or	10:23:02
16		neutral thermal conditions, we chose to deprotect the	10:23:05
17		modified oligonucleotides using methanolic ammonia at	10:23:11
18		room temperature."	10:23:15
19		Do you see that? Did I read it correctly?	10:23:17
20	A	Yes.	10:23:20
21	Q	Then it goes on to say "Under the usual	10:23:21
22		oligonucleotide deprotection conditions (concentrated	10:23:25
23		NH4OH at 55 degrees Celsius), we in fact observed	10:23:29
24		significant degradation of the	10:23:34
25		2 prime-deoxy-2-prime-fluoropyrimidine nucleosides	10:23:36

1	while the nucleosides were stable to methanolic	10:23:43
2	ammonia at room temperature."	10:23:47
3	Did I read that correctly?	10:23:49
4	A Yes.	10:23:51
5	Q So doesn't Kawasaki identify a degradation	10:23:51
6	problem with 2 prime-deoxy 2-prime-fluoro nucleosides?	10:24:01
7	A That is immediately solved in the same	10:24:06
8	sentence.	10:24:09
9	Q But we can talk about that. We can talk	10:24:09
10	about that. But I'm asking doesn't it identify a	10:24:13
11	problem?	10:24:16
12	A It identifies a problem which is immediately	10:24:18
13	solved in the same sentence. That's my answer.	10:24:21
14	Q Okay. And then what is the solution to the	10:24:23
15	problem?	10:24:26
16	A To use methanolic ammonia.	10:24:26
17	Q But you wouldn't be able to use these	10:24:37
18	compounds with methylamine, correct?	10:24:40
19	A I mean, you might be able to use methylamine	10:24:43
20	in a certain solvent system.	10:24:52
21	Q But isn't it fair to say that there are	10:25:00
22	limitations associated with deprotecting	10:25:03
23	2 prime-deoxy-2-prime-fluoropyrimidine nucleosides	10:25:09
24	based on Kawasaki and other references?	10:25:15
25	A No. In terms of the POSA desiring to get a	10:25:18

1	final compound, it would be clear from this paper that	10:25:25
2	they should probably use methanolic ammonia for their	10:25:28
3	deprotection.	10:25:33
4	Q But a POSA would also know to stay away from	10:25:34
5	methylamine?	10:25:39
6	A Well, the paper just says ammonium hydroxide	10:25:43
7	is a problem. I don't see where it says methylamine	10:25:48
8	is a problem.	10:25:51
9	Q And the NH ₄ OH is aqueous ammonia; is that	10:25:55
10	correct?	10:27:01
11	A Correct.	10:27:01
12	Q So your testimony is they observed the	10:27:03
13	problem when using aqueous ammonia, right?	10:27:06
14	A My testimony is, just reading the paper,	10:27:13
15	that's what they say.	10:27:15
16	MR. SHORES: Okay. You can take that down.	10:27:59
17	And if we can put up Exhibit 1019.	10:28:10
18	THE TECHNICIAN: Stand by.	10:28:33
19	(Baran Exhibit 1019 marked for	10:28:34
20	identification.)	10:28:48
21	Q I would assume you're familiar with this	10:28:48
22	paper?	10:28:51
23	A Yes, sir.	10:28:51
24	Q Okay. And this is Exhibit 1019, which is	10:28:52
25	the Fan reference; is that right?	10:28:55

1	A	Correct.	10:28:58
2	Q	So your testimony was that the deprotection	10:29:00
3		conditions in Fan were chosen intentionally to slow	10:29:04
4		down the reactions to compare isobutyryl and acetyl,	10:29:10
5		correct?	10:29:17
6	A	Yes.	10:29:17
7	Q	Where in Fan does it state that?	10:29:17
8	A	Well, it's implied here, right here on page	10:29:30
9		2. [As read]: "To compare the" -- "To compare	10:29:33
10		deprotection rates of the guanine N-isobutyryl,	10:29:37
11		acetyl, and phenoxy groups, 9 micromole samples of 6a,	10:29:41
12		6b, and the corresponding isobutyryl derivative were	10:29:46
13		dissolved in a 1.4 milliliter solution that was 1.3	10:29:51
14		percent methylamine, 2.6 percent ethanol, and 96	10:29:55
15		percent methylene chloride by weight."	10:29:58
16		So that's why, because it says here "to	10:30:01
17		compare deprotection rates." They clearly are using a	10:30:05
18		set of conditions here that is completely exogenous	10:30:08
19		and not reflective of what you would do in SPOS.	10:30:12
20	Q	Right. In your testimony you just	10:30:17
21		identified, you know, in your declaration, you omitted	10:30:21
22		the phenoxyacetyl group as one of the -- the groups to	10:30:27
23		compare, correct?	10:30:32
24	A	Okay.	10:30:33
25	Q	Do you agree?	10:30:36

1	A	I mean, if that's -- if it's omitted from --	10:30:37
2		if it's omitted from the declaration, then that's what	10:30:40
3		it is, sure.	10:30:44
4	Q	I mean, here in this Table 1, it shows	10:30:45
5		phenoxyacetyl as being significantly faster than	10:30:52
6		acetyl, right?	10:30:58
7	A	It is.	10:30:59
8	Q	So a POSA reading this would have been	10:31:00
9		motivated to use PAC rather than acetyl, right, if	10:31:04
10		they're going for speed?	10:31:10
11	A	Not necessarily. The problem with PAC, the	10:31:13
12		reason it's not used as much, is it's -- it is perhaps	10:31:15
13		too labile in certain cases.	10:31:18
14	Q	Well, isn't it true that PAC is known as a	10:31:20
15		-- was known, at the time of this paper and also at	10:31:24
16		the time of the 2009 time frame, that PAC was a	10:31:28
17		well-known option for protecting guanine-based	10:31:35
18		nucleosides?	10:31:39
19	A	There were a lot of protecting groups that	10:31:41
20		are known for protecting nucleosides. And the reason	10:31:44
21		that someone might want to pick acetyl over	10:31:47
22		phenoxyacetyl could be due to a variety of factors.	10:31:51
23		It could be due to minimizing the molecular weight.	10:31:55
24		It could be due to commercial availability of building	10:31:59
25		blocks. It could be due to the own practitioner's	10:32:03

1	experience in terms of deprotection rates on their	10:32:09
2	scaffold of interests. And it could be that they view	10:32:12
3	the acetyl as being the kind of Goldilocks; not too	10:32:17
4	fast, not too slow.	10:32:21
5	Q Wouldn't you agree that acetyl is smaller	10:32:24
6	group than phenoxyacetyl?	10:32:28
7	A Of course.	10:32:31
8	Q And wouldn't you agree that having	10:32:32
9	phenoxyacetyl attached to compound X would have made	10:32:37
10	compound X more soluble in organic solvents than	10:32:45
11	acetyl?	10:32:50
12	A No, I don't know that.	10:32:51
13	Q Phenoxyacetyl is more hydrophobic than	10:32:52
14	acetyl, though, right?	10:33:05
15	A But you have to take into account the entire	10:33:06
16	-- the properties of the bulk material. This myopic	10:33:09
17	obsession with solubility is misplaced and is not	10:33:12
18	within the rubric of how a POSA thinks about making	10:33:16
19	oligonucleotides.	10:33:20
20	Q You know, as a matter of basic textbook	10:33:21
21	chemistry, when you have compound X that has acetyl	10:33:27
22	attached to the N2 position of guanine versus compound	10:33:31
23	X with phenoxyacetyl attached to the N2 position of	10:33:34
24	guanine, isn't it true that the compound X with the	10:33:39
25	acetyl is less soluble in organic solvents than	10:33:45

1	compound X with phenoxyacetyl?	10:33:50
2	A Maybe. What I'm saying is it's irrelevant	10:33:54
3	because a POSA would look at it and it wouldn't be a	10:33:58
4	gating step for them. They wouldn't -- they would	10:34:02
5	pick their end protecting group based on other	10:34:02
6	concerns, not based on relative solubilities, because	10:34:05
7	there's nothing about using acetyl versus	10:34:08
8	phenoxyacetyl or isobutyryl that a POSA would be,	10:34:11
9	like, oh, I can't use this group or that group because	10:34:13
10	I'm not going to be able to dissolve it in NMP or	10:34:16
11	acetonitrile in order to use it on my synthesizer.	10:34:23
12	That wouldn't be part of the consideration for a POSA.	10:34:25
13	MR. SHORES: Take this down, please.	10:34:31
14	Thanks, Jack.	10:34:33
15	Q Dr. Baran, during your September 13th, 2023	10:34:40
16	deposition I had asked you whether you had conducted	10:34:44
17	any tests relating to adding acetic anhydride in step	10:34:50
18	2 of example 4D of the '031 patent, and you said you	10:34:58
19	did not conduct tests; is that correct?	10:35:02
20	A I didn't do any experimental work for this	10:35:03
21	case.	10:35:06
22	Q And then when I asked you whether Hongene	10:35:07
23	had conducted those tests, you said you didn't know.	10:35:15
24	Do you remember that?	10:35:18
25	A That's correct. I still don't know.	10:35:18

1	Q	Okay. Yeah, that was my question is since	10:35:20
2		that time have you gained knowledge one way or the	10:35:23
3		other as to whether Hongene has conducted the subject	10:35:26
4		tests or not?	10:35:31
5	A	I have no idea.	10:35:32
6	Q	Have you ever asked them?	10:35:34
7	A	No.	10:35:35
8		MR. SHORES: Okay. I think we're at a good	10:35:49
9		breaking point, if that's okay with you, Dr. Baran.	10:35:52
10		THE WITNESS: Whatever you like.	10:35:55
11		MR. SHORES: Come back in 10 minutes?	10:35:57
12		THE WITNESS: Sure.	10:36:00
13		THE VIDEOGRAPHER: We are going off the	10:36:00
14		record at 10:35 a.m.	10:36:01
15		(Recess 10:36 a.m. - 10:50 a.m.)	10:36:04
16		THE VIDEOGRAPHER: We are going back on the	10:50:36
17		record at 10:50 a.m.	10:50:42
18		MR. SHORES: Dr. Baran, if we can pull up --	10:50:46
19		I guess, Jack, if you can pull up Exhibit 1033.	10:50:48
20		THE TECHNICIAN: Yes. Stand by.	10:50:55
21		BY MR. SHORES:	10:50:55
22	Q	Dr. Baran, we're pulling your declaration	10:50:59
23		back up. If we can go to paragraphs 94 to 106, so I	10:51:01
24		guess just go to 94. Okay. And you see this -- you	10:51:17
25		provided testimony with respect to Ground III relating	10:51:30

1	to the structural differences between compound 5 and	10:51:35
2	claim 2 of the '885, right?	10:51:40
3	A Yes.	10:51:43
4	Q Confirming that you did not apply the lead	10:51:44
5	compound analysis in connection with Ground III,	10:51:51
6	correct?	10:51:58
7	MR. EDWARDS: Object to form.	10:51:58
8	A I didn't apply lead compound analysis for	10:52:10
9	any of these reagents.	10:52:13
10	Q Okay. That's what I wanted to confirm.	10:52:15
11	So you did not apply the lead compound	10:52:18
12	analysis in any of the opinions that you provided in	10:52:21
13	Exhibit 1033, your declaration, correct?	10:52:26
14	A I mean, I have a section talking about -- is	10:52:31
15	this the reply declaration? Yeah, this is the reply.	10:52:34
16	Q Yes.	10:52:37
17	A Yeah, I have a section on the lead compound	10:52:38
18	analysis, and I don't think it's relevant to	10:52:41
19	considering reagents.	10:52:44
20	Q Right. So your testimony is you did not	10:52:48
21	apply that analysis to your opinions in this case,	10:52:51
22	correct?	10:52:59
23	A It's addressed in my reply declaration, to	10:53:01
24	the extent that I considered it. We can go to that	10:53:04
25	section, if you want, where it talks about it.	10:53:09

1 Q Sure. I mean, my question is pretty 10:53:12
2 straightforward, is did you apply the lead compound 10:53:16
3 analysis in this case or not? 10:53:19

4 MR. EDWARDS: And his request is 10:53:23
5 straightforward, to see that section. 10:53:25

6 MR. SHORES: Okay. 10:53:31

7 A Which section should I go to? 10:53:32

8 Q The section where you testified that you 10:53:40
9 discussed the lead compound analysis. 10:53:44

10 A I guess we have to go to the TLC first -- 10:53:49
11 here we go. Yeah, here we go, page 6. 10:53:54

12 This is where I talk about and consider the 10:54:06
13 lead compound analysis and framework. 10:54:09

14 Q Okay. So is it your testimony that your 10:54:12
15 opinion is that the lead compound framework does not 10:54:15
16 apply to this case? 10:54:18

17 A Correct. 10:54:22

18 Q Okay. And, therefore, you did not apply it 10:54:23
19 to this case? 10:54:26

20 A Correct. 10:54:27

21 Q Okay. Thank you. 10:54:28

22 MR. SHORES: Okay. We can take this down. 10:54:33

23 So to Jeremy, we're going to introduce some 10:54:42
24 of the documents that were produced recently. So I 10:54:48
25 want to give you the opportunity to, I guess, if 10:54:54

1 you're still holding or maintaining the position that 10:54:58
2 those are attorneys' eyes only related documents, then 10:55:03
3 -- is that your position? I guess I'm confirming 10:55:08
4 that. 10:55:12

5 MR. EDWARDS: Yeah. So if you're going to 10:55:12
6 pull them up, we should excuse the ChemGenes personnel 10:55:15
7 from this portion of the deposition. And I'll mark it 10:55:20
8 as, you know, attorneys' eyes only under the 10:55:22
9 Protective Order or designate it that. 10:55:26

10 MR. SHORES: Okay. So Adam and I will stay 10:55:31
11 on. And then Anuj, Kevin, Jeremy, Yann, I just ask 10:55:33
12 you, respectfully, to sign off for this portion of the 10:55:42
13 deposition. 10:55:45

14 MR. O'CONNOR: Oh, okay. Thank you 10:55:55
15 everyone. Take care. Thanks. 10:55:58

16 (Kevin O'Connor, Anuj Mohan Srivastava, 10:56:03
17 Jeremy Little and Yann Thillier disconnect from the 10:56:03
18 Zoom proceeding.) 10:56:05

19 (The following portion from 96:22 to 159:11 10:56:05
20 was designated Confidential - Attorneys' Eyes only 10:56:05
21 pursuant to Protective Order.) 10:56:06

22 MR. SHORES: So, Jeremy, you've designated 10:56:06
23 the transcript? 10:56:09

24 MR. EDWARDS: Well, hang on -- 10:56:10

25 MR. SHORES: Not the whole transcript, but 10:56:12

1	this -- this section of it. I just want you to have	10:56:13
2	the opportunity, that's all.	10:56:16
3	MR. EDWARDS: Yeah, I mean, you haven't said	10:56:17
4	anything yet. But in anticipation --	10:56:19
5	MR. SHORES: Right.	10:56:19
6	MR. EDWARDS: -- of that, I would, yes,	10:56:21
7	so...	10:56:24
8	MR. SHORES: Okay.	10:56:24
9	BY MR. SHORES:	10:56:44
10	Q Dr. Baran, in your opening declaration,	10:56:45
11	which is dated January 18th, 2023, you testified that	10:56:48
12	you were retained by Procopio and compensated at \$750	10:56:56
13	an hour for this case, right?	10:57:09
14	A Correct.	10:57:11
15	Q And again, that was January 18th, 2023?	10:57:12
16	A I guess so. I don't remember the dates. I	10:57:16
17	trust you.	10:57:18
18	Q When did you -- so that declaration was	10:57:19
19	submitted it's dated January 18, 2023.	10:57:25
20	When did you start working on that	10:57:32
21	declaration?	10:57:34
22	A Permission to use my email?	10:57:35
23	Q Sure.	10:57:37
24	A Let me search for first contact with Jeremy,	10:57:44
25	see if I have that.	10:57:48

1	First contact with Jeremy was May 13 --	10:58:01
2	Friday, May 13, 2022, that was first contact with	10:58:04
3	Jeremy --	10:58:09
4	Q Okay.	10:58:09
5	A -- and Procopio. And then the work began in	10:58:10
6	earnest in June, June of 2022.	10:58:14
7	Q Okay. And when were you first retained	10:58:20
8	formally with -- in connection with this case?	10:58:26
9	A Let's see. It looks like the executed	10:58:32
10	document was -- attached is a fully executed	10:58:35
11	agreement -- fully executed agreement on May 25th of	10:58:40
12	2022.	10:58:45
13	Q And then the -- you were being retained and	10:58:46
14	was -- were you being retained for multiple cases?	10:58:51
15	Like what case were you being retained for?	10:58:54
16	A The current case -- let's see. The email	10:58:57
17	here are three -- let's see.	10:59:01
18	THE WITNESS: Jeremy, can I read the first	10:59:06
19	email, or is that secret?	10:59:08
20	MR. EDWARDS: No, you can't read it.	10:59:10
21	What he wants to know is whether you were	10:59:12
22	retained initially at the outset for all three IPRs,	10:59:17
23	for something less, for something more, for something	10:59:26
24	broader. If I may, Dan, I think that's what --	10:59:29
25	MR. SHORES: Yeah, exactly.	10:59:33

1	BY MR. SHORES:	10:59:34
2	Q I don't want to know what your	10:59:34
3	communications were, just the facts.	10:59:35
4	And then also one question would be were you	10:59:37
5	retained for the District Court case or is it just	10:59:41
6	these IPRs?	10:59:45
7	A I think the best person to ask so you get an	10:59:46
8	accurate answer is Jeremy. I mean --	10:59:49
9	MR. EDWARDS: So if I may step in a little	10:59:51
10	bit, Phil. It's also possible that it's not clear to	10:59:53
11	you from what you're trying to look at right here on	10:59:57
12	the fly. So those are possibilities I don't know.	10:59:59
13	THE WITNESS: Yeah. I see three patents	11:00:02
14	that you put in the initial email of May 13, but --	11:00:04
15	Q In the agreement -- in the retainer	11:00:09
16	agreement, is there a matter that's identified?	11:00:11
17	A Let me look. Let me find that email.	11:00:16
18	Expert agreement. Retainer agreement. It says scope,	11:00:26
19	consultant to the client.	11:00:32
20	It doesn't really say -- it just calls it --	11:00:42
21	here it is. Regarding ChemGenes Corporation versus	11:00:49
22	Hongene Biotechnology Ltd., United States District	11:00:53
23	Court for the District of Massachusetts, Case Number	11:00:58
24	1:22-cv-10290-PBS, and any related inter partes	11:01:02
25	reviews of these patents asserted by ChemGenes.	11:01:11

1	That's the front line on the retainer agreement.	11:01:15
2	Q Okay. Thank you.	11:01:17
3	And so that retainer agreement is dated May	11:01:18
4	25, 2022?	11:01:21
5	A May 24 is what the Word document shows.	11:01:23
6	Q Okay. And so as of that date, May 24th,	11:01:27
7	2022, had you as -- individually, ever had -- did you	11:01:31
8	have a relationship with Hongene at that point?	11:01:38
9	A No, aside from running into people at	11:01:40
10	conferences, and, you know, using them as a vendor to	11:01:45
11	buy stuff. Probably bought stuff from ChemGenes, too.	11:01:49
12	Q So in terms of when you bought stuff from	11:01:55
13	Hongene, that was -- you're talking about the	11:01:58
14	companies that you're affiliated with, right?	11:02:01
15	A No, no. I'm saying as a researcher myself	11:02:03
16	or the lab or one of the companies I'm affiliated with	11:02:07
17	bought reagents from all the vendors out there. Like	11:02:12
18	a relationship, no, I didn't have any relationship	11:02:18
19	with Hongene --	11:02:21
20	Q Okay. I'm sorry. I don't mean to	11:02:23
21	interrupt.	11:02:25
22	So I'm trying to understand, so you have --	11:02:25
23	you're a researcher and you work at Scripps, right?	11:02:29
24	You wear a lot of hats, right?	11:02:33
25	So, but -- so you're at Scripps, and you're	11:02:35

1 talking about in your capacity at Scripps you were -- 11:02:37
2 you bought, you know, reagents, for example, from 11:02:41
3 Hongene? 11:02:43

4 A Perhaps. We bought from -- I'm pretty sure 11:02:44
5 the lab had purchased from ChemGenes, Hongene, Glen. 11:02:47
6 I mean, that's like that's my -- there's 40 people in 11:02:54
7 the lab and a lot of people do various oligonucleotide 11:02:59
8 research. So I don't monitor who buys what and where 11:03:04
9 they buy it from; I'm just assuming. That would be the 11:03:10
10 extent of any relationship I had with them, if you 11:03:11
11 call it a relationship. 11:03:13

12 Q Yeah. So, I mean, there's different ways 11:03:14
13 you define professional relationship, right? 11:03:16

14 One -- you're defining it here as of May 24, 11:03:18
15 2022, where your -- if I understand, your testimony is 11:03:22
16 that your recollection is that the only, quote, 11:03:26
17 "relationship" that you had with Hongene at that time 11:03:31
18 was utilizing them as a vendor and then seeing some of 11:03:33
19 their employees at conferences and so forth, right? 11:03:39

20 A That's it. And probably ChemGenes and Glen 11:03:43
21 and -- you know, I go to an oligonucleotide conference 11:03:46
22 and give a talk in front of an audience of 500 people, 11:03:51
23 and some people at the end come up and ask questions 11:03:51
24 or we chat, and it's hard for me to remember who they 11:03:55
25 are. 11:03:58

1	Q	Right. And so you never, as an individual,	11:03:58
2		entered into any contract discussions or agreement	11:04:02
3		discussions with Hongene as of May 24th, 2022?	11:04:09
4	A	No.	11:04:13
5	Q	Okay. And then what about as -- what about	11:04:15
6		Elsie, as a co-founder of Elsie, did Elsie have an	11:04:19
7		existing relationship with Hongene as of May 24th,	11:04:27
8		2022?	11:04:30
9	A	Not to my knowledge beyond, again, buying	11:04:31
10		stuff from them and every other vendor.	11:04:34
11	Q	And did Elsie contemplate a relationship	11:04:37
12		with Hongene at that time? Was there any licensing	11:04:41
13		discussions or agreement discussions that Elsie had	11:04:44
14		with Hongene at that time --	11:04:47
15	A	Never.	11:04:55
16	Q	What about polyARNA?	11:04:56
17	A	No.	11:04:58
18	Q	No agreement with Hongene as of May 24th,	11:04:58
19		2022?	11:05:02
20	A	Not at all.	11:05:03
21	Q	No negotiations or licensing discussions or	11:05:04
22		agreement discussions with between polyARNA and	11:05:11
23		Hongene as of May 24th, 2022?	11:05:15
24	A	No. And in fact, only a handful of people	11:05:18
25		even knew the company existed.	11:05:21

1	Q	When you say "the company," you're talking	11:05:22
2		about polyARNA?	11:05:25
3	A	Correct.	11:05:27
4	Q	At that time, yeah.	11:05:27
5		And then what about Nutcracker?	11:05:29
6	A	I'm just a member of their scientific	11:05:31
7		advisory board. I have no idea -- I don't even know	11:05:33
8		where they buy their stuff from.	11:05:36
9	Q	And what about Scripps and Hongene, the	11:05:42
10		relationship between Scripps and Hongene other than as	11:05:47
11		a vendor?	11:05:50
12	A	I'm not aware of any -- to my knowledge,	11:05:51
13		there is no relationship with Hongene at all.	11:05:54
14	Q	As of May 24th, 2022?	11:05:58
15	A	Yeah, even up to today, I'm not aware of any	11:06:01
16		relationship they have with the --	11:06:04
17	Q	With Scripps?	11:06:11
18	A	-- with the institute, right.	11:06:12
19	Q	And then you testified during your January	11:06:25
20		22nd, 2024 deposition that you were appointed to	11:06:30
21		Hongene's advisory board, right?	11:06:36
22	A	As of what date? Sorry?	11:06:40
23	Q	Yeah. So we recall that the last time that	11:06:45
24		we were together on a Zoom call it was on January	11:06:49
25		22nd, 2024, and we had a deposition in connection with	11:06:54

1	the '569 and '707 IPRs. Do you recall?	11:06:59
2	A Yes, I recall.	11:07:04
3	Q And then during that deposition you	11:07:04
4	testified that you were -- you had been appointed to	11:07:08
5	Hongene's advisory board, right?	11:07:13
6	A Correct, and I provided all the documents	11:07:15
7	you requested.	11:07:18
8	Q And when did those discussions begin?	11:07:25
9	Meaning when did those discussions with you as an	11:07:31
10	individual serving on Hongene's advisory board, when	11:07:35
11	did those begin?	11:07:40
12	A It's, again, you have all the emails, I	11:07:41
13	assume.	11:07:44
14	Q Well, I have what was produced.	11:07:46
15	A I gave you everything. I forwarded all the	11:07:49
16	emails I had regarding the Hongene SAB to Jeremy, who	11:07:51
17	I assume forwarded them all to you.	11:07:57
18	I don't -- off the top of my head, don't	11:07:58
19	recall the exact date, but you have the date. I think	11:08:00
20	initial contact was made in like January of last year,	11:08:06
21	but it wasn't regarding an SAB. It was just a --	11:08:09
22	There's a lot of background noise. I don't	11:08:13
23	know if someone wants to mute.	11:08:16
24	Q Yeah, that's not me. Okay.	11:08:18
25	All right. Yeah. Okay. So you just don't	11:08:22

1	-- sitting here without the document in front of you,	11:08:24
2	you're not -- you can't say for sure.	11:08:27
3	MR. SHORES: So let's look -- let's pull up	11:08:30
4	Exhibit 2033.	11:08:32
5	(Baran Exhibit 2033 marked for	11:08:57
6	identification.)	11:09:03
7	Q Okay. Do you see this exhibit, Dr. Baran?	11:09:03
8	A Oh, yes. Mm-hmm.	11:09:05
9	Q And you recognize this document?	11:09:06
10	A Yes, I do.	11:09:09
11	Q Okay. What is -- what is it?	11:09:10
12	A It's a first contact with the chief	11:09:15
13	technology officer with -- of Hongene. And the email	11:09:18
14	is self-explanatory.	11:09:24
15	Do you want me to read it?	11:09:26
16	Q No, that's okay. I just -- you're saying	11:09:27
17	"first contact." So does that mean that you've never	11:09:31
18	heard from David Butler before?	11:09:37
19	A Well, you can read the first paragraph of	11:09:40
20	the email. Apparently, I did meet him before. I	11:09:43
21	didn't recall, but I meet -- when I visit places and	11:09:46
22	go to conferences and go to companies, I meet	11:09:48
23	thousands of people and I just don't have a great	11:09:52
24	memory to remember every single person I met.	11:09:55
25	So apparently, he says here -- maybe it's	11:09:58

1 good to read it. It says, "I'm not sure whether you 11:10:01
2 remember me..." And to tell you parenthetically, I 11:10:03
3 didn't. He said, "I used to be the head of chemistry 11:10:07
4 at Wave. You were kind enough to give a 11:10:10
5 presentation...." blah, blah, blah. And he was there 11:10:14
6 apparently, so I suppose I met him. 11:10:17

7 In fact, when we did our Zoom or Teams 11:10:19
8 meeting for the first time, I didn't remember him, but 11:10:22
9 apparently I did meet him. 11:10:25

10 Q Okay. So you don't remember meeting him. 11:10:27
11 But, you know, the best of your recollection, this was 11:10:32
12 really your first contact with him on a professional 11:10:36
13 level. Is that fair to say? 11:10:42

14 A I have no other emails from David Butler. I 11:10:44
15 searched. 11:10:49

16 Q Okay. I understand that you don't have any 11:10:53
17 other emails. But I'm asking to the best of your 11:10:56
18 recollection, this was the first time that you had 11:10:58
19 heard from David Butler prior to -- 11:11:00

20 A That is correct. 11:11:11

21 Q Yeah. Okay. And then here he's saying on 11:11:12
22 the bottom, "In one way, shape or form I'd love to get 11:11:17
23 you involved in what we're doing at Hongene and am 11:11:22
24 keen to discuss potential opportunities for us to work 11:11:26
25 together if you can spare some time in the coming 11:11:28

1	days."	11:11:31
2	Did I read that correctly?	11:11:32
3	A Yeah.	11:11:34
4	Q And do you recall whether you replied to	11:11:34
5	him?	11:11:37
6	A I did.	11:11:38
7	Q Okay.	11:11:42
8	A I thought that was forwarded as well in one	11:11:44
9	of the other emails.	11:11:46
10	Q We don't have that.	11:11:50
11	A Oh, really? Just give me a second, I'll	11:11:52
12	read to you what I wrote to him.	11:11:55
13	David Butler -- let's see, this email is	11:12:02
14	dated January 20. Let me go January 20 --	11:12:03
15	MR. SHORES: Jeremy, we would like this	11:12:07
16	produced.	11:12:09
17	THE WITNESS: I'll forward it to Jeremy	11:12:10
18	right now. Just give me a second -- or I'll forward	11:12:12
19	it to you. Whatever Jeremy tells you to do is fine.	11:12:15
20	MR. EDWARDS: Well, you should forward it to	11:12:18
21	me.	11:12:20
22	MR. SHORES: Yeah.	11:12:20
23	MR. EDWARDS: Dan, I can tell you that we've	11:12:20
24	produced everything that was provided by Dr. Baran and	11:12:23
25	his administrative assistant except for the slide	11:12:28

1	presentation because you weren't asking for it at the	11:12:34
2	time.	11:12:37
3	MR. SHORES: Yeah. We would like a copy of	11:12:39
4	that as well, that's part of my -- would be part of my	11:12:40
5	request. I've noticed that in one of the headers of	11:12:44
6	the email it wasn't provided, so I would ask you to	11:12:48
7	please produce that also.	11:12:50
8	MR. EDWARDS: Okay. I'll have to take that	11:12:54
9	to the client, because the understanding at the time,	11:12:57
10	based on our discussions and correspondence, was you	11:13:00
11	were not requesting that in advance of this	11:13:03
12	deposition.	11:13:06
13	THE WITNESS: Okay. I just forwarded it to	11:13:08
14	Jeremy. I can share my screen, if you want. I can --	11:13:10
15	I just forwarded it to Jeremy and I can read --	11:13:10
16	MR. SHORES: Ask Jeremy about that.	11:13:15
17	MR. EDWARDS: Well, let me take a look at	11:13:16
18	it. Okay.	11:13:18
19	THE WITNESS: I can read it to you. It's	11:13:19
20	one line. Do you want me to read it to you?	11:13:21
21	MR. EDWARDS: That's fine.	11:13:24
22	THE WITNESS: Okay. It says, "Sure, Dave.	11:13:26
23	That would be great. Shelly can set up a time to	11:13:27
24	Zoom. Best, Phil."	11:13:33
25	BY MR. SHORES:	11:13:35

1	Q	Okay. Thank you, Dr. Baran.	11:13:35
2	A	Sure.	11:13:38
3	Q	And did you -- do you recall speaking with	11:13:38
4		David Butler following this email exchange?	11:13:41
5	A	I don't remember exactly, but it looks like	11:13:46
6		I have a Zoom meeting that was scheduled for Thursday,	11:13:50
7		January 26 at 8:15 a.m. Pacific time.	11:13:55
8	Q	And did you send any other emails to David	11:14:00
9		Butler or receive any other emails from David Butler	11:14:05
10		between January 20th and January 26th?	11:14:10
11	A	No. I'm searching the "To David Butler" on	11:14:12
12		the Outlook folder here. And I've only got -- I've	11:14:16
13		only got the one to him and cc Shelly, and then Shelly	11:14:20
14		scheduled a time, and then the next time we met was	11:14:25
15		over Zoom on the 26th.	11:14:28
16	Q	And if you -- if you go to --	11:14:46
17		MR. SHORES: We need to pull up Exhibit	11:14:55
18		2036, please.	11:14:58
19		(Baran Exhibit 2036 marked for	11:15:00
20		identification.)	11:15:29
21	Q	Do you see this document, Dr. Baran?	11:15:29
22	A	Yes.	11:15:32
23	Q	Do you recognize it?	11:15:32
24	A	I recognize one of the emails I sent to	11:15:33
25		Jeremy.	11:15:36

1 Q Okay. And if you go to the first email, 11:15:36
2 which is on the second page, so it would be the first 11:15:42
3 in time, May 17th, 2023. 11:15:45
4 A Yes. 11:15:48
5 Q I'll read the email, or part of the email 11:15:49
6 into the record. 11:15:57
7 It says, "Hi Phil, Apologies for the delay 11:15:57
8 since we last spoke, I've been getting used to the new 11:16:02
9 role and drinking from the firehose. Back in January 11:16:06
10 we had an excellent initial discussion around the 11:16:09
11 following topics: 11:16:12
12 "1. Areas for collaboration. 11:16:13
13 "2. Assembly of a Hongene advisory board. 11:16:16
14 "3. Licensing of [REDACTED] from [REDACTED] 11:16:20
15 "Sub 1. After your connection, initial 11:16:25
16 discussions with [REDACTED] were promising but [REDACTED] 11:16:28
17 [REDACTED]. Am following up with [REDACTED]." 11:16:32
18 Did I read that correctly? 11:16:36
19 A Yes. 11:16:38
20 Q And point 4 says, "Getting a CDA in place 11:16:38
21 (this was completed)." 11:16:42
22 Did I read that correctly? 11:16:44
23 A Yes. 11:16:45
24 Q Okay. So is it your understanding that the 11:16:46
25 "excellent initial discussion" that David Butler 11:16:52

1	identifies that occurred back in January was this	11:16:55
2	January 26th meeting?	11:16:59
3	A Yes.	11:17:03
4	Q And do you now recall that as part of that	11:17:03
5	January 26 meeting, you discussed the assembly of a	11:17:09
6	Hongene advisory board?	11:17:13
7	A It was one of the topics he broached, but I	11:17:16
8	had no idea what that entailed.	11:17:19
9	Q Okay. So what did he -- do you remember	11:17:23
10	what he -- what was discussed surrounding the advisory	11:17:26
11	board assembly?	11:17:35
12	A Just, like, well, we're thinking of starting	11:17:35
13	an SAB and, you know, something in principle you might	11:17:38
14	be interested in. And I said, sure, you know, depends	11:17:41
15	on what the time commitment is, what the compensation	11:17:43
16	is, what do you want, kind of was my question because	11:17:45
17	I don't know what they want.	11:17:49
18	Q Right. And this is something that they	11:17:50
19	broached with you, not that you brought up with them,	11:17:53
20	correct?	11:17:55
21	A Correct.	11:17:56
22	Q "They" being Hongene, right?	11:17:59
23	A Correct.	11:18:02
24	Q And then this was May 17, 2023. And do you	11:18:18
25	recall when you entered into the formal agreement to	11:18:30

1	serve on the Hongene advisory board?	11:18:36
2	A No, I have no reason to recall that. I sent	11:18:39
3	you all the emails and --	11:18:42
4	(Simultaneous speaking.)	11:18:45
5	Q All right. Let's make it easy.	11:18:45
6	MR. SHORES: Let's go to Exhibit 2037.	11:18:48
7	(Baran Exhibit 2037 marked for	11:19:13
8	identification.)	11:19:23
9	Q Okay. And you see this document, Dr. Baran?	11:19:23
10	A Yeah.	11:19:26
11	Q And you recognize it?	11:19:26
12	A Yeah.	11:19:28
13	Q What is it?	11:19:29
14	A This is an email where David is sending a	11:19:30
15	draft of the contract and I'm basically saying, yeah,	11:19:35
16	I skimmed, it looked fine to me. And as part of the	11:19:39
17	process of my employment at Scripps, the legal	11:19:42
18	department here has to review and make sure that I'm	11:19:46
19	in compliance.	11:19:52
20	Q Universities and institutions tend to do	11:19:52
21	that, don't they?	11:19:55
22	A Correct.	11:19:56
23	MR. SHORES: So if we can pull up Exhibit	11:20:02
24	2034.	11:20:06
25	Q Actually, before we do that, the -- if you	11:20:08

1 can look at the email dated July 24th, 2023. 11:20:12

2 A Which one? There's a couple. 11:20:17

3 Q Yeah, I'm sorry. Down the bottom of page -- 11:20:20

4 the first page. 9 -- Hongene_0000009. 11:20:23

5 It says -- and this is from David Butler to 11:20:36

6 you, correct? 11:20:40

7 A Yeah. 11:20:41

8 Q And it says, "Attached is a draft contract 11:20:42

9 for you for the Hongene advisory board. I hope the 11:20:48

10 terms are to your satisfaction, we did our best to 11:20:52

11 achieve [REDACTED] 11:20:57

12 [REDACTED], albeit with [REDACTED] as 11:21:01

13 discussed when we talked on the phone a couple of 11:21:04

14 weeks ago." 11:21:07

15 Did I read that correctly? 11:21:08

16 A Yes. 11:21:09

17 Q What types of financial arrangements did you 11:21:10

18 discuss with David Butler relating to service on the 11:21:14

19 advisory board? 11:21:18

20 A Well, he -- he told me that some of the 11:21:21

21 advisors preferred [REDACTED] 11:21:23

22 [REDACTED] 11:21:27

23 [REDACTED]. And my standard agreement for serving 11:21:30

24 on an SAB and giving my time is to be compensated for 11:21:38

25 my time because my lab won't be doing work on this 11:21:42

1	effort.	11:21:50
2	Q Right. So this was a relationship with you	11:21:51
3	as an individual and you requested cash compensation,	11:21:54
4	correct?	11:22:00
5	A Correct.	11:22:01
6	Q Was the -- did you discuss -- ever discuss	11:22:02
7	with Hongene [REDACTED] ?	11:22:12
8	A No.	11:22:16
9	Q Did Hongene ever bring that up with you,	11:22:20
10	[REDACTED] ?	11:22:23
11	A No.	11:22:26
12	Q Did Hongene ever bring up with you that a	11:22:26
13	potential form of [REDACTED] ?	11:22:31
14	A No.	11:22:35
15	Q And are you aware of how the other members	11:22:35
16	of the advisory board are being compensated?	11:22:41
17	A I am not.	11:22:44
18	Q Did Hongene ever indicate that Hongene was	11:22:47
19	compensating the other members of the advisory board	11:22:52
20	[REDACTED] ?	11:22:56
21	A No.	11:22:59
22	Q Are you aware if anyone else on the advisory	11:22:59
23	board is being compensated in cash?	11:23:06
24	A No.	11:23:09
25	Q So you don't know -- so do you know what the	11:23:09

1	compensation arrangement is with anyone else on the	11:23:13
2	advisory board?	11:23:15
3	A I did not ask.	11:23:16
4	Q So do you know?	11:23:17
5	A I do not know.	11:23:18
6	Q So it's possible they are also being paid	11:23:27
7	cash; you just don't know one way or the other?	11:23:30
8	A Correct.	11:23:34
9	MR. SHORES: Okay. If we can pull up	11:23:36
10	Exhibit 2034.	11:23:37
11	THE TECHNICIAN: Stand by.	11:23:50
12	(Baran Exhibit 2034 marked for	11:23:52
13	identification.)	11:24:10
14	Q Do you see this document, Dr. Baran?	11:24:10
15	A Yes.	11:24:12
16	Q And you recognize it?	11:24:12
17	A Yes.	11:24:14
18	Q Okay. And what is it?	11:24:15
19	A It's the advisor agreement for serving on	11:24:17
20	the SAB.	11:24:20
21	Q Okay. And when did you sign this advisor	11:24:20
22	agreement?	11:24:26
23	A I assume it's the effective date of August	11:24:30
24	7th, but maybe -- maybe it was in July, but I'm not	11:24:33
25	sure. It's probably in one of the emails I sent you.	11:24:36

1	Maybe it's on the signature page at the end here.	11:24:40
2	Let's see. Looks like - I don't see a date	11:24:44
3	here. Oh, yeah. It looks like 8/7, around August 7th	11:24:55
4	probably.	11:25:00
5	Q Okay. On or around August 7th?	11:25:01
6	A Yeah, that's what it looks like.	11:25:04
7	Q Looks like that's when you signed -- you and	11:25:08
8	Scripps -- yeah, you and Scripps signed it around	11:25:11
9	then, but doesn't look like there's a date on when --	11:25:18
10	if you go to 0000036, the effective date of the	11:25:21
11	agreement is August 7th.	11:25:32
12	A 7 or 8, because there's other people who	11:25:35
13	signed on the 8th.	11:25:38
14	Q If you go to Section 1 of the advisor	11:25:39
15	agreement, it says, "Description of Services. Advisor	11:25:42
16	will provide consulting services to company as agreed	11:25:54
17	to from time to time by the parties, including	11:25:58
18	attending company's advisory board meetings no less	11:26:02
19	than three times per year."	11:26:06
20	Did I read that correctly?	11:26:08
21	A Yes.	11:26:10
22	Q So what -- what have you done in connection	11:26:10
23	with the advisory board since August 7th, 2023?	11:26:20
24	A Done brainstorming, had calls with David to	11:26:28
25	think about, you know, bounce ideas what he might have	11:26:34

1	had on topics for what the next SAB should cover, or	11:26:40
2	in one case there was a pressing problem, a chemical	11:26:44
3	consulting problem they needed help with. It's that	11:26:47
4	kind of thing.	11:26:51
5	He'll email me when he needs help and I'll	11:26:52
6	provide, you know, expert advice on how to solve a	11:26:55
7	tricky chemical problem, or a high level, you know,	11:26:59
8	what do you think we should cover on the next SAB. Or	11:27:03
9	a week before the SAB meeting they'll send the slides	11:27:06
10	and the slides will have questions and then I'll do	11:27:09
11	research and due diligence to make sure I'm prepared	11:27:11
12	for that meeting. That kind of thing.	11:27:14
13	Q So about how much time, you know, have	11:27:18
14	you -- have you put toward the advisory board so far?	11:27:23
15	A Maybe -- maybe 20 hours or so; 10, 20 hours,	11:27:30
16	something like that, including the meeting times.	11:27:38
17	Q Yeah. And has there been any discussion --	11:27:41
18	well, let me go back.	11:27:51
19	So the term of this agreement is one year,	11:27:53
20	correct?	11:27:56
21	A Correct.	11:27:57
22	Q So, and if I'm reading this contract	11:27:58
23	correctly in section 2, it says, "unless either party	11:28:03
24	provides to the other party 30 days' prior written	11:28:11
25	notice of its desire to not automatically renew this	11:28:14

1 agreement" -- excuse me. Let me read the full
2 sentence.

3 "Furthermore, this agreement will
4 automatically renew at the end of the initial term and
5 each term thereafter for one additional year, unless
6 either party provides to the other party 30 days'
7 prior written notice of its desire not to
8 automatically renew this agreement."

9 Did I read that correctly?

10 A Yes, you did.

11 Q Okay. Have you had any discussions with
12 Hongene relating to [REDACTED]

13 [REDACTED]?

14 A No.

15 Q Do you expect that you will continue to
16 serve on the advisory board after the initial one-year
17 term is concluded, which appears to be August 7th,
18 2024?

19 A I see no reason why -- why it won't
20 continue. But, you know, I've served on a lot of SABs
21 in my time and I don't have any expectations because
22 companies have, you know, issues which are external,
23 that are not necessarily associated with performance.

24 So I have been on SABs and everything is
25 going great, and all of a sudden their financials look

1	terrible and they need to cut everything and they fire	11:29:47
2	people and they eliminate their SAB.	11:29:49
3	So I don't have any expectations. I just do	11:29:52
4	my job. I could be fired from Scripps.	11:29:55
5	Q This -- this agreement here, this advisor	11:30:06
6	agreement, indicates that Hongene agreed to pay you	11:30:10
7	\$70,000 per year for your services; is that correct?	11:30:20
8	A Correct.	11:30:29
9	Q And then Hongene, under this agreement, is	11:30:29
10	to provide payment of \$17,500 per calendar quarter; is	11:30:35
11	that correct?	11:30:46
12	A That's what it says.	11:30:46
13	Q So have you received any payment from	11:30:47
14	Hongene or -- let me ask a different way.	11:30:49
15	After this agreement was entered into on	11:30:55
16	August 7, 2023, did you receive any payment from	11:30:59
17	Hongene?	11:31:01
18	A I did at the end of last year.	11:31:02
19	Q And was that the -- was it one payment?	11:31:09
20	A Yes.	11:31:13
21	Q And is that the only payment that you've	11:31:13
22	received from Hongene so far?	11:31:17
23	A Correct.	11:31:19
24	Q And what was the total of that payment?	11:31:19
25	A 17,500.	11:31:21

1	Q	And when do you expect the next payment?	11:31:26
2	A	I guess one calendar month after the first	11:31:31
3		quarter. I don't really keep track. I suppose maybe	11:31:36
4		April or something.	11:31:41
5	Q	Okay. And you were deposed in this case in	11:31:42
6		September 2023, right? Do you recall that?	11:31:58
7	A	Yes.	11:32:01
8	Q	And then at the time of that September 13,	11:32:02
9		2023 deposition, you were separately engaged with	11:32:10
10		Hongene in this advisor agreement, under which Hongene	11:32:19
11		agreed to pay you \$70,000 per year to serve on its	11:32:23
12		advisory board, correct?	11:32:29
13	A	Correct.	11:32:32
14	Q	And you recall that at the beginning of that	11:32:32
15		September 13, 2023 deposition, you agreed to provide	11:32:40
16		full, truthful, and complete testimony?	11:32:48
17	A	Yes.	11:32:51
18	Q	And then you also recall that you testified	11:32:52
19		that you reviewed your declaration over the weeks	11:32:58
20		leading up to the September 13th, 2023 deposition and	11:33:02
21		you noticed a typo.	11:33:07
22		Do you remember that?	11:33:09
23	A	Yes.	11:33:10
24	Q	And then do you remember you alerted me to	11:33:11
25		about that typo which went into the record?	11:33:14

1	A	Yes.	11:33:17
2	Q	But you didn't alert me about your \$70,000	11:33:18
3		contract with Hongene that had been entered into a	11:33:25
4		month earlier, correct?	11:33:28
5	A	Correct. There's a lot of SABs where I get	11:33:29
6		paid money to provide services.	11:33:32
7	Q	And then in connection with this case, you	11:33:41
8		submitted a second reply declaration, which we've	11:33:44
9		looked at today, Exhibit 1033, correct?	11:33:52
10	A	Yeah.	11:33:55
11	Q	And that declaration was dated January 19th,	11:33:56
12		2024, right?	11:34:02
13	A	Yes.	11:34:03
14	Q	But you didn't disclose your	11:34:06
15		\$70,000-per-year contract with Hongene in your January	11:34:12
16		19th, 2024 declaration, right?	11:34:16
17	A	I didn't think it was relevant. Jeremy knew	11:34:21
18		about the SAB. None of us thought it was relevant to	11:34:24
19		the facts of the case because my obligations to the	11:34:27
20		SAB have nothing to do with this case.	11:34:31
21	Q	So you discussed with counsel whether you	11:34:36
22		should include it or not?	11:34:39
23	A	I just alerted --	11:34:40
24		MR. EDWARDS: Object to form and instruct	11:34:41
25		not to answer. That's privileged communication, work	11:34:43

1	product, et cetera.	11:34:45
2	MR. SHORES: That's not privileged.	11:34:46
3	MR. EDWARDS: Disagree. You have my	11:34:48
4	instruction.	11:34:50
5	MR. SHORES: Okay.	11:34:50
6	MR. EDWARDS: Next question.	11:34:55
7	BY MR. SHORES:	11:35:02
8	Q But you didn't disclose this \$70,000-a-year	11:35:03
9	contract with Hongene in your January 19th, 2024	11:35:08
10	declaration, correct?	11:35:14
11	A No.	11:35:16
12	Q Can you go back to -- if we can go back to	11:35:16
13	Exhibit 2036.	11:36:42
14	And do you see this email, Dr. Baran?	11:37:02
15	A Yes.	11:37:04
16	Q And this email indicates that there was a	11:37:05
17	CDA that was completed between you and Hongene; is	11:37:12
18	that right?	11:37:17
19	A That's what it says.	11:37:17
20	Q Is that -- did that happen?	11:37:19
21	A Permission to check my email?	11:37:21
22	Q Sure.	11:37:24
23	A Yes, it did.	11:37:46
24	Q What was the date of that agreement?	11:37:49
25	A "Please find attached fully executed CDA."	11:37:52

1	It is Thursday, February 9th, 2023.	11:37:55
2	MR. SHORES: Okay. We would like a copy of	11:38:00
3	that.	11:38:02
4	THE WITNESS: Let me forward it right now to	11:38:05
5	Jeremy. One second.	11:38:07
6	MR. SHORES: Yeah, my request is to Jeremy.	11:38:10
7	THE WITNESS: Okay. Forwarded it to Jeremy	11:38:13
8	right now.	11:38:18
9	Q Do you recall during your January 22, 2024	11:38:20
10	deposition, I asked you: "And do you have any other	11:38:39
11	agreements with Hongene besides the agreement you	11:38:46
12	referenced earlier that relates to the service on the	11:38:49
13	advisory board?"	11:38:52
14	And you testified "No."	11:38:53
15	Do you remember that?	11:38:57
16	A Yes.	11:38:58
17	Q So that wasn't true, was it?	11:38:58
18	A Well, I mean, it's legalese because I	11:39:01
19	thought that the SAB contract supercedes all previous	11:39:06
20	stuff. And a CDA is just basically a permission to	11:39:10
21	speak freely. So if you consider that a contract,	11:39:14
22	then, okay, and I just sent it to you.	11:39:17
23	There's nothing to hide here.	11:39:20
24	Q Sitting here today, do you have any other	11:39:33
25	agreements with Hongene besides the advisor agreement	11:39:38

1	and CDA?	11:39:44
2	A Not that I'm aware of.	11:39:45
3	Q So it's possible you have other agreements	11:39:53
4	with Hongene?	11:39:55
5	A There are none that I'm aware of. I can	11:39:56
6	search again my email and see if there's anything.	11:39:59
7	But I don't think there's anything aside from the	11:40:02
8	contract, and then a CDA, which I'm not a lawyer, I	11:40:05
9	didn't consider that to be a contract. It's just -- I	11:40:09
10	sign CDAs all the time with people and -- that are	11:40:11
11	just basically a permission to speak freely. But it's	11:40:13
12	not a contract because it doesn't involve any payment	11:40:17
13	or anything other than, hey, we can tell you a secret	11:40:22
14	and you can tell us a secret and you don't disclose it	11:40:26
15	to anybody else.	11:40:29
16	So aside from those -- from the CDA and the	11:40:30
17	contract, I'm not aware of other documents I signed	11:40:33
18	with Hongene.	11:40:36
19	Q Okay. Well, we would like you to check	11:40:41
20	that --	11:40:44
21	A Okay. Give me a second.	11:40:45
22	Q -- and confirm.	11:40:47
23	A Okay. Let's see. Draft advisor, contract	11:40:49
24	press release -- no, I don't think there's anything,	11:41:01
25	no. There's nothing. There's a CDA and there's a	11:41:04

1 contract, that's it. 11:41:08

2 Q That has to do with you as an individual? 11:41:22

3 A Yeah, just permission to talk and not worry 11:41:25

4 about secrecy. 11:41:29

5 MR. SHORES: And if we can go to Exhibit 11:41:52

6 2036. Is that what we have here or what is this one? 11:41:55

7 MR. EDWARDS: I think you're on it. 11:42:01

8 MR. SHORES: -- 2036. 11:42:07

9 Q One of the items that Dr. -- I mean that 11:42:07

10 David Butler -- Dr. Butler raised with you under point 11:42:14

11 3 was the licensing of [REDACTED] from [REDACTED] 11:42:20

12 Do you see that? 11:42:25

13 A Yes. 11:42:26

14 Q And what was the subject of that discussion? 11:42:26

15 A They wanted to find out how feasible it 11:42:32

16 would be to license [REDACTED] so that 11:42:36

17 they could [REDACTED] and things using that -- 11:42:41

18 incorporate that [REDACTED]. 11:42:46

19 Q And the [REDACTED], that's the entire [REDACTED] 11:42:52

20 [REDACTED] 11:42:58

21 A Well, they wanted [REDACTED], the 11:42:58

22 ability to [REDACTED] that have the [REDACTED] 11:43:01

23 [REDACTED]. And as you recall, that's really 11:43:07

24 the sole reason why David contacted me back in January 11:43:10

25 of that year. 11:43:14

1 Q And here it says "licensing of [REDACTED] 11:43:18
2 from [REDACTED] correct? 11:43:25

3 A Correct. 11:43:29

4 Q And that's -- and that's because at that 11:43:31
5 time -- why is that? 11:43:37

6 I mean, [REDACTED] had the rights to sublicense the 11:43:39
7 technology; is that correct? 11:43:43

8 A Correct. They [REDACTED] 11:43:43

9 [REDACTED]. 11:43:47

10 Q And then what is meant by 3 sub 1, "After 11:43:56

11 your connection, initial discussions with [REDACTED] were 11:44:01

12 promising but [REDACTED]. Am 11:44:06

13 following up with [REDACTED]," what does that mean? 11:44:10

14 A They talked to [REDACTED] and [REDACTED] was excited 11:44:13

15 to have it done, but [REDACTED] is a very, very big company 11:44:17

16 and their legal is just overwhelmed with stuff, so 11:44:20

17 they were very slow to get back to him. 11:44:23

18 And then he was following up with [REDACTED] who 11:44:26

19 is an employee at [REDACTED] because [REDACTED] has certain 11:44:29

20 rights -- commercial rights to [REDACTED]. And so he was 11:44:33

21 going to follow up with [REDACTED] and see if they can work 11:44:37

22 with [REDACTED] who might be faster than [REDACTED] 11:44:41

23 Q So who is [REDACTED] 11:44:47

24 A [REDACTED]. 11:44:49

25 Q And where does he work? 11:44:52

1	A	[REDACTED].	11:44:58
2	Q	And where does [REDACTED] work?	11:44:59
3	A	[REDACTED]	11:45:05
4	Q	Okay. And so you connected David with	11:45:06
5	[REDACTED]		11:45:16
6	A	Correct.	11:45:17
7	Q	And then you also connected him with [REDACTED]	11:45:18
8	A	Correct.	11:45:20
9		MR. SHORES: We would like a copy of that	11:45:30
10		email -- all communications relating to -- relating to	11:45:32
11		Dr. Baran's connecting David Butler with [REDACTED] and	11:45:42
12	[REDACTED]		11:45:49
13	A	Okay. One second. I have the [REDACTED] email,	11:45:51
14		I'm forwarding that to Jeremy right now.	11:45:53
15		Let me see about [REDACTED] One second.	11:46:00
16		The only email I have -- I think -- I think	11:47:33
17		I might have just given [REDACTED] email to David over the	11:47:37
18		Zoom or he may have known [REDACTED] from an oligo	11:47:41
19		conference. I don't have an email intro like I do	11:47:46
20		for -- for introducing David with [REDACTED] I think	11:47:51
21		he -- either he already knew [REDACTED] from a conference or	11:47:55
22		I just gave him [REDACTED] email. But I don't have an	11:48:00
23		email like the one you'll see that I sent to [REDACTED]	11:48:03
24		doing a formal introduction.	11:48:06
25	Q	Okay. So what is the subject of the -- I	11:48:11

1	think you started to talk about it, but like you	11:48:17
2	developed the P(V) or at least part of the P(V)	11:48:21
3	platform at Scripps, right?	11:48:27
4	A Yeah. It was collaboratively developed with	11:48:29
5	Bristol-Myers.	11:48:33
6	Q Right. And Bristol-Myers funded -- provided	11:48:34
7	funding, is that right, for the research?	11:48:36
8	A Yes.	11:48:39
9	Q Yeah. And then are you aware -- are you	11:48:39
10	aware of -- let me pull that back.	11:48:51
11	So with BMS, BMS has certain	11:48:53
12	commercialization rights over that --	11:49:00
13	A Correct.	11:49:02
14	Q -- technology?	11:49:03
15	A Yes.	11:49:05
16	Q And we talked earlier that BMS has -- I'm	11:49:06
17	sorry.	11:49:13
18	At your last deposition, we discussed that	11:49:13
19	BMS sublicenses that technology to MilliporeSigma; is	11:49:17
20	that correct?	11:49:27
21	A Only for reagent sales.	11:49:27
22	Q Right. And does any of that -- does Elsie	11:49:31
23	have a license to any of that technology?	11:49:40
24	A Yes, they do.	11:49:43
25	Q Is it from BMS?	11:49:44

1	A	Yes.	11:49:46
2	Q	So what -- what can Elsie do with that	11:49:49
3		technology? What are the parameters of how it can use	11:49:54
4		P(V) that was developed at Scripps?	11:49:59
5	A	They have rights to use it in a commercial	11:50:01
6		setting, nonexclusive rights to -- and sublicensing	11:50:04
7		rights.	11:50:10
8		So let's say, for example, they collaborate	11:50:11
9		with a company, the company has an oligonucleotide	11:50:13
10		they want to commercialize and they want to make it	11:50:19
11		with the PSI reagent, they can do so while working	11:50:25
12		with Elsie.	11:50:29
13	Q	And Elsie sublicenses the patents --	11:50:32
14		(Simultaneous speaking.)	11:50:52
15	A	Yes.	11:50:52
16	Q	-- in that circumstance?	11:50:53
17		And is Elsie developing other of its own	11:50:55
18		homegrown technologies?	11:51:01
19	A	Yeah, as we discussed in January, quite a	11:51:03
20		few.	11:51:07
21	Q	Right. And then that would be Elsie's to do	11:51:07
22		with it what it wants?	11:51:11
23	A	Correct.	11:51:14
24	Q	Does the sublicense that Elsie -- does the	11:51:15
25		sublicense that Elsie's able to provide need BMS'	11:51:35

1	approval?	11:51:40
2	A No. They have a contract, and as long as	11:51:48
3	they fit within the parameters of that contract, they	11:51:50
4	don't need approval. I believe there are some	11:51:54
5	royalties and a certain percentage that goes back to	11:51:57
6	BMS. So they don't -- they have the contract, they	11:52:03
7	don't need permission anymore.	11:52:04
8	Q When you say "anymore," what do you mean?	11:52:06
9	A Well, in the very beginning of the company,	11:52:08
10	there was a lot of discussion about, you know, do we	11:52:11
11	need permission for each target; does it need to be by	11:52:17
12	target. Like, when we were formulating the contract,	11:52:22
13	we were -- you know, there was a lot of discussions	11:52:24
14	like how was this going to work.	11:52:26
15	When the contract and various amendments	11:52:28
16	were formalized, now we don't need, you know, to ping	11:52:32
17	them every time we want to do something and say, hey,	11:52:37
18	is this okay, is that okay? As long as we operate	11:52:40
19	within the bounds of the contract and the amendments	11:52:45
20	thereof, we're fine.	11:52:46
21	Q When you say "they" and "we" you're talking	11:52:47
22	about Elsie?	11:52:50
23	A Correct.	11:52:51
24	Q And so was there an amendment made to the	11:52:52
25	agreement between Elsie and BMS?	11:52:54

1	A	There have been various amendments over the	11:52:57
2		past year or two.	11:52:59
3	MR. SHORES:	Okay. If we can go to Exhibit	11:53:20
4		2038, please.	11:53:24
5		(Baran Exhibit 2038 marked for	11:53:49
6		identification.)	11:53:51
7	Q	Dr. Baran, do you see this email?	11:53:51
8	A	Yes.	11:53:54
9	Q	And do you -- do you recognize it?	11:53:54
10	A	Yes.	11:54:02
11	Q	Okay. What is it, please?	11:54:03
12	A	It's, I guess, a follow-up to the first SAB	11:54:05
13		meeting we had on -- you know, time to brainstorm	11:54:10
14		together with Professor Damha, you know, new -- new	11:54:17
15		products.	11:54:23
16	Q	Okay. And this is an email from David	11:54:27
17		Butler to you and Masad Damha?	11:54:33
18	A	Uh-huh, yes.	11:54:38
19	Q	What is Dr. Damha's role here?	11:54:42
20	A	He's another member of the SAB. He's a	11:54:46
21		well-known professor in oligonucleotide chemistry at	11:54:49
22		McGill. Some of the references are in this case.	11:54:53
23	Q	And Dr. -- I'm sorry, yeah, when I say	11:54:57
24		David Butler, but Dr. Butler -- David Butler says in	11:55:03
25		this email, "On a related topic, I met with [REDACTED] and	11:55:06

1 [REDACTED] at [REDACTED] recently. To update you both on that, 11:55:09
2 below are their notes and action items for Hongene 11:55:13
3 arising from that meeting." 11:55:17

4 Did I read that correctly? 11:55:18

5 A Yes. 11:55:20

6 Q And [REDACTED] is [REDACTED]? 11:55:20

7 A Yes. 11:55:22

8 Q And who is [REDACTED] 11:55:23

9 A That's [REDACTED], he's the chief operating 11:55:25
10 officer. 11:55:29

11 Q Okay. And then the first line says, "[REDACTED] 11:55:30
12 expects to have a fully executed agreement with [REDACTED] by 11:55:37
13 EOY that will provide full access to the [REDACTED] 11:55:42

14 Did I read that correctly? Did I read it 11:55:47
15 correctly? 11:55:51

16 A Yes, you did. 11:55:51

17 Q Okay. Sorry. I just didn't hear so I 11:55:53
18 wanted to make sure I wasn't muffled out or something. 11:55:57

19 And what -- what is meant by "a fully 11:56:06
20 executed agreement with [REDACTED] What's the agreement? 11:56:08

21 A To -- more broad ability to use -- to 11:56:13
22 sublicense [REDACTED] and other -- other scenarios as well 11:56:19
23 such as [REDACTED]. 11:56:26

24 Q So what was the motivation to reach this 11:56:30
25 agreement? I mean, would [REDACTED] have the ability to 11:56:34

1 make more money?

11:56:39

2 A No. I think that the main goal and the
3 reason, you know, the scientists at [REDACTED] supported as
4 well, is simply to democratize access to the [REDACTED]
5 [REDACTED]. As I think I told you many times last time,
6 reagent sales are not a recipe for economic success
7 for a biotech.

11:56:41

11:56:45

11:56:50

11:56:56

11:57:00

11:57:06

8 Q So what -- [REDACTED] now has the ability to
9 you're saying more broadly sublicense the [REDACTED], right?

11:57:16

11:57:22

10 A That was the hope then.

11:57:27

11 Q That was the hope then.

11:57:31

12 Where do these -- where does it stand now?
13 Was the agreement executed?

11:57:40

11:57:43

14 A I believe we're -- where it settled was that
15 they would just work with Sigma-Aldrich directly with
16 the preexisting contract that exists.

11:57:45

11:57:48

11:57:52

17 Hongene offered the materials to sell,
18 that's it. And [REDACTED] interest is only having more
19 people use the [REDACTED]. Eventually, I
20 mean, one of the motivations is sort of altruistic
21 because we know the chemistry is really good and it
22 can help people.

11:57:55

11:57:57

11:58:03

11:58:08

11:58:13

11:58:15

23 And one of the motivations is potentially
24 economic. Because if you think about it, from a
25 standpoint of, okay, let's think five years from now,

11:58:17

11:58:19

11:58:21

1 10 years from now, if many people are using [REDACTED] 11:58:24
2 there's a chance that one company would say, oh, we've 11:58:28
3 identified our oligonucleotide therapeutic, we need to 11:58:33
4 use [REDACTED] to manufacture, we need a commercial license 11:58:37
5 to operate to make a metric ton. And then they would 11:58:41
6 perhaps then go to [REDACTED] and say, hey, let's discuss 11:58:45
7 economic terms. 11:58:48

8 Does that make sense? 11:58:50

9 Q Well, here's what I'm trying to understand 11:58:51
10 is, you had testified that there were discussions -- 11:58:55
11 there were discussions at least as of November 27, 11:59:01
12 2023, and then also dating back to May 2023, 11:59:04
13 surrounding [REDACTED] ability to sublicense the [REDACTED] 11:59:21
14 technology. 11:59:34

15 A For reagent sales. 11:59:34

16 Q And your testimony is that that license is 11:59:35
17 limited to reagent sales. Is that your testimony? 11:59:47

18 A No. I think we're confusing a lot of 11:59:51
19 things. So Elsie has a commercial -- a license to 11:59:54
20 operate commercially or sublicense to partners that 12:00:01
21 they work with for the scale-up of an oligonucleotide 12:00:05
22 that uses PSI in its manufacture. That's one piece. 12:00:09
23 Let's separate that from the reagent piece. 12:00:13

24 The other pieces are reagents which the sale 12:00:16
25 of reagents is licensed to Sigma-Aldrich, and people 12:00:19

1 can buy reagents from Aldrich, they can use it for 12:00:25
2 research and development -- research only. They can't 12:00:29
3 use it for commercial applications. 12:00:31

4 [REDACTED] was trying also to get that ability in 12:00:33
5 order to simply speed up the process, because working 12:00:35
6 directly with [REDACTED] and their lawyers is very 12:00:38
7 cumbersome. And so that was the -- that's the story. 12:00:42

8 Q And so the aspect that -- so [REDACTED] can 12:00:48
9 sublicense [REDACTED] independent of the reagent piece, they 12:00:52
10 can do it relating to the manufacturing? 12:01:00

11 I guess can you clarify that? 12:01:03

12 A Yeah. So if -- let's say if they have a 12:01:04
13 candidate oligonucleotide therapeutic and they use [REDACTED] 12:01:07
14 to make it -- 12:01:11

15 Q I'm sorry to interrupt. But when you say 12:01:12
16 "they," just so the record is clear, who are we 12:01:14
17 talking about? 12:01:17

18 A I'll start over. Let's say Elsie identifies 12:01:18
19 a therapeutic in-house and Elsie would like to 12:01:22
20 commercialize it. They can -- "they" as in Elsie, can 12:01:26
21 do that. Let's imagine that they partner with a big 12:01:30
22 company. Big company X wants to make their 12:01:33
23 therapeutic using PSI technology. That company can do 12:01:37
24 it because they're working with Elsie. 12:01:41

25 This is different than a reagent for 12:01:45

1	exploratory purposes.	12:01:48
2	Q Like similar to the deal with Glaxo?	12:02:00
3	In other words, that -- doesn't Elsie have a	12:02:04
4	deal with Glaxo?	12:02:08
5	A They have a deal with Glaxo. But what do	12:02:10
6	you mean "similar to the deal with Glaxo"?	12:02:14
7	Q Meaning -- I mean, we talked about Elsie	12:02:16
8	having certain rights relating to the P(V) technology,	12:02:18
9	one of them was relating to reagents, and then the	12:02:22
10	other had to do with what you just described, which is	12:02:27
11	Elsie working with company X to license its P(V)	12:02:33
12	technology for a therapeutic, for example.	12:02:37
13	And so my question was, is that the type of	12:02:39
14	deal you have with -- Elsie has with Glaxo?	12:02:42
15	A No. I think you can refer back to my	12:02:46
16	deposition testimony from last month. The deal we	12:02:49
17	have with Glaxo is a collaboration deal to field test	12:02:52
18	the Rosalind platform, that's what we spent all that	12:02:59
19	time working on. And in the future, it may be that	12:03:04
20	GSK wants to commercialize an oligonucleotide that	12:03:08
21	requires the use of PSI. And in that case, they would	12:03:12
22	have the advantage of being able to operate with	12:03:17
23	Elsie's commercial license.	12:03:22
24	But what we did with GSK during that initial	12:03:24
25	collaboration period that the press release was given	12:03:29

1 on was not for P(V) chemistry. 12:03:31

2 Q Right. That's a different -- that's what I 12:03:34
3 was asking. I understand that you had testified to 12:03:36
4 this in the other proceeding, but I was just, I guess, 12:03:38
5 confirming. 12:03:41

6 So do you have any -- so let me go back. 12:03:43

7 So relative to your -- these discussions, so 12:03:46
8 is it fair that to say you had -- you were having 12:03:52
9 discussions or [REDACTED] was having discussions with 12:03:55
10 [REDACTED] about a potential collaboration in November 12:03:58
11 2023? 12:04:08

12 A I don't know if it would be -- I mean, it 12:04:11
13 depends on how you define collaboration. I think it 12:04:14
14 was more of just like a brainstorming of how do we get 12:04:16
15 these reagents out to more people. And [REDACTED] -- it's 12:04:20
16 in [REDACTED] best interest to do that for the long term. 12:04:25

17 The short term, there's no financial gain to 12:04:29
18 be had for reagent sales. And it's long term, like, 12:04:34
19 okay, how do we get this into more people's hands? 12:04:39
20 Because Sigma-Aldrich is very slow; they're often 12:04:43
21 back-ordered. They're not very adept in the 12:04:47
22 oligonucleotide space. Whereas, [REDACTED] 12:04:51
23 [REDACTED]. 12:04:56

24 And so that's -- [REDACTED] is sort of 12:04:58
25 brainstorming and trying to facilitate and helping 12:05:02

1	this [REDACTED]	12:05:08
2	[REDACTED].	12:05:11
3	Q So this potential collaboration with [REDACTED]	12:05:16
4	was -- your testimony is it was an opportunity to	12:05:21
5	democratize the reagents and that's in [REDACTED]	12:05:26
6	long-term interest, correct?	12:05:32
7	A Correct.	12:05:33
8	Q So what was the actual deal with [REDACTED]	12:05:35
9	Was it -- you're saying it's limited to reagents?	12:05:45
10	MR. EDWARDS: Object to form.	12:05:48
11	A I mean, I don't -- I don't think anything	12:05:51
12	has been signed, maybe a CDA -- probably a CDA is in	12:05:53
13	place between the two parties. I don't think there's	12:05:58
14	any kind of contract other than a CDA that I'm aware	12:06:00
15	of.	12:06:03
16	The deal is what I told you, like, [REDACTED]	12:06:04
17	trying to be friendly and in their best interest to	12:06:07
18	try to get the [REDACTED] into more hands of	12:06:10
19	oligonucleotide chemists.	12:06:15
20	Q And there's no -- there's no money involved?	12:06:19
21	A As of right now, there's no money, no.	12:06:22
22	Q Okay. So as of right now is there an	12:06:25
23	agreement in place between [REDACTED] and [REDACTED]	12:06:30
24	A There is probably a CDA.	12:06:33
25	Q Okay. We're going to need a copy of the	12:06:39

1	CDA.	12:06:41
2	A I don't know if I can provide that.	12:06:41
3	Q Well, I'm asking counsel --	12:06:42
4	A You need to, you know, subpoena or whatever	12:06:48
5	you need to do with --	12:06:48
6	Q I'm not asking you, Dr. Baran. I'm asking	12:06:49
7	Jeremy.	12:06:54
8	We would also need the contract between --	12:06:56
9	in all these agreements that have been discussed	12:06:58
10	between Elsie and BMS.	12:07:01
11	A Elsie and BMS, I don't know if I can give	12:07:05
12	you any of that. You'll have to work directly with	12:07:07
13	Elsie.	12:07:11
14	Q Yeah, there's mechanisms for that.	12:07:12
15	A Great.	12:07:16
16	MR. EDWARDS: Dan, I would request that you	12:07:17
17	send me a list rather than an ad hoc verbal request in	12:07:20
18	the deposition.	12:07:23
19	I'll note that you've now gone -- we've had	12:07:24
20	quite a bit of patience with this complete sideshow,	12:07:27
21	and you've now gone to try to metastasize this into	12:07:31
22	involving third parties, et cetera. So please send me	12:07:34
23	the list, the justification, and we're going to have	12:07:39
24	the draw the line here. This can't spin out the way	12:07:42
25	that you seem to be wanting it to.	12:07:45

1 MR. SHORES: The speaking objection is not 12:07:49
2 appropriate. And I disagree with your 12:07:51
3 characterization of the questions relating to 12:07:53
4 Dr. Baran's bias and his undisclosed financial 12:07:59
5 relationships with [REDACTED] 12:08:05

6 MR. EDWARDS: It's not an objection. It's a 12:08:08
7 response to your request and a request to put it in 12:08:10
8 writing and justify it -- 12:08:12

9 (Simultaneous speaking.) 12:08:12

10 MR. SHORES: -- speech, it's just not 12:08:15
11 appropriate. 12:08:17

12 MR. EDWARDS: Well, neither is making 12:08:19
13 discovery requests at this stage during a deposition. 12:08:21
14 You're wasting Dr. Baran's time in many ways. 12:08:24

15 Please proceed with the rest of your 12:08:27
16 questioning of the witness. 12:08:30

17 MR. SHORES: Well, I will if I'm not 12:08:31
18 interrupted by you. 12:08:34

19 MR. EDWARDS: You interrupted yourself to 12:08:35
20 launch a bunch of vague discovery requests involving 12:08:36
21 third parties. Please proceed with your deposition. 12:08:41

22 MR. SHORES: Are you finished? Okay. 12:08:49

23 BY MR. SHORES: 12:09:05

24 Q So what is the status of the negotiations 12:09:06
25 between [REDACTED] and [REDACTED] today? 12:09:09

1 MR. EDWARDS: Object to form. Foundation. 12:09:12
2 Mischaracterizing. 12:09:14

3 A They're -- there is no negotiation. I think 12:09:18
4 they are just friendly -- they're just having friendly 12:09:20
5 conversation. As I've told you, there's no money 12:09:24
6 changing hands. There's no contract that I'm aware 12:09:27
7 of. 12:09:30

8 But you can depose all the people at [REDACTED] 12:09:32
9 This is as relevant as deposing my mortgage broker to 12:09:35
10 find out what my terms are on my mortgage. You can 12:09:39
11 check my DNA, urine samples, whatever you like, sir; 12:09:42
12 it's all irrelevant. But you can depose everybody. 12:09:47

13 MR. SHORES: Move to strike the witness' 12:09:51
14 answer as nonresponsive. 12:09:53

15 A I responded. I think it's all funny. 12:09:57

16 Q On Exhibit 2038, so if we look at Exhibit 12:10:09
17 2038, there's a statement that says [As read]: "[REDACTED] 12:10:15
18 expects to have a fully executed agreement with [REDACTED] by 12:10:20
19 end of year that will provide full access to the [REDACTED] 12:10:22
20 [REDACTED]." 12:10:26

21 Did I read that correctly? 12:10:27

22 A Yeah. 12:10:28

23 Q Was that contract executed? 12:10:29

24 A I don't think it got done in time. 12:10:33

25 Q So you're saying you don't know one way or 12:10:36

1	the other?	12:10:40
2	A I'm saying to my knowledge I don't think it	12:10:40
3	was actually completed by the end of the year. I	12:10:43
4	think -- yeah.	12:10:46
5	Q Okay. Is it completed sitting here today?	12:10:49
6	A I don't -- I think they had a completed	12:10:52
7	agreement but not for the part that is [REDACTED] As	12:10:57
8	far as I heard, the last I heard -- I don't keep up	12:11:00
9	with this too much. The last I heard was that [REDACTED]	12:11:02
10	decided to work directly with [REDACTED],	12:11:07
11	[REDACTED] whatever they're called.	12:11:12
12	So they ended up -- I think contractually	12:11:17
13	they ended up not working with [REDACTED] on this at all.	12:11:20
14	I think it's now a collaboration with [REDACTED] and	12:11:23
15	[REDACTED]	12:11:27
16	Q So you're saying you know that for a fact or	12:11:28
17	are you saying that's your --	12:11:32
18	A I'm almost sure that's my current	12:11:33
19	understanding. But, yeah, again, we can, you know,	12:11:36
20	depose everybody.	12:11:39
21	Q Well, no one is suggesting that. I'm just	12:11:41
22	looking to get answers to these questions.	12:11:44
23	MR. SHORES: So if we go to Exhibit 2039.	12:11:50
24	(Baran Exhibit 2039 marked for	12:11:58
25	identification.)	12:12:24

1 Q And if you look at the email, I guess it's 12:12:24
2 on Hongene 0000013, dated -- there's an email from 12:12:27
3 David Butler to you and others dated October 22, 2023. 12:12:33

4 Do you see that? 12:12:39

5 A Yup. 12:12:39

6 Q And then if you go to the next page, which 12:12:49
7 is Hongene 14, there's a heading that says 12:12:55

8 "[REDACTED]." 12:13:04

9 Do you see that? 12:13:07

10 A Yes. 12:13:08

11 Q And sub 1, it says, "We will pursue 12:13:08
12 potential to [REDACTED] with [REDACTED] now 12:13:11
13 that they have reached a good point with licensing 12:13:14
14 negotiations with [REDACTED] 12:13:18

15 Do you see that? 12:13:20

16 A Yes. 12:13:21

17 Q What does that refer to? 12:13:21

18 A Well, that's earlier in history when they 12:13:23
19 were thinking they could work with [REDACTED] to get that 12:13:26
20 license to operate with [REDACTED] But that -- I don't 12:13:32
21 think that ended up working out. I think what they're 12:13:37
22 now doing -- if you want, I can just shoot an email to 12:13:42
23 David Butler or Jeremy, can ask him, whatever -- I 12:13:47
24 think what they are doing is working with [REDACTED] -- 12:13:52
25 it's [REDACTED] 12:13:53

1 Q When you say "they," you're talking about 12:13:54
2 Hongene? 12:13:56

3 A Yeah. [REDACTED] doesn't care about the reagent 12:13:57
4 sales at all. They have no interest in the finances 12:14:01
5 of selling a dinky reagent. They couldn't care less. 12:14:07
6 They were trying to do this just to, as I said many 12:14:11
7 times, make it more available to the public. 12:14:15

8 I think the conclusion as of this year was 12:14:17
9 favorable terms to just work directly with 12:14:20
10 [REDACTED]. [REDACTED] was the key -- key 12:14:24
11 contact there that they worked with. And I have no 12:14:28
12 relationship with [REDACTED] 12:14:33

13 Q So your testimony is, sitting here today, 12:14:54
14 [REDACTED] and [REDACTED] have not entered into an agreement, 12:14:59
15 correct? 12:15:04

16 A Well, if you're going to again catch me on a 12:15:05
17 CDA, they may have signed a CDA. I don't think that's 12:15:10
18 an agreement. But whatever you're defining as an 12:15:14
19 agreement, there's probably a CDA. 12:15:17

20 Q Okay. I'm not trying to catch you. I'm 12:15:19
21 just trying to understand the relationship between 12:15:21

22 [REDACTED] and [REDACTED] 12:15:23

23 And so it's -- 12:15:24

24 A Well, let's be -- let's be fair, you know, 12:15:26
25 everything is about trying to catch me in some nuance. 12:15:28

1 So I got to be careful that you're not trying to do 12:15:32
2 that. 12:15:35

3 So I don't know of any agreement that -- 12:15:35
4 that [REDACTED] and [REDACTED] have, aside from what is 12:15:37
5 probable of a CDA, but I don't even know if that 12:15:42
6 exists either. 12:15:45

7 Q Okay. I'm not trying to catch you. I'm 12:15:47
8 truthfully not trying to do that. I'm trying to 12:15:49
9 understand the relationship. 12:15:52

10 And so when -- just to give you context, so 12:15:53
11 professional relationships are defined by contracts, 12:15:56
12 right? So you have a CDA, which is, you know, there's 12:16:00
13 a purpose for the CDA and that defines a relationship 12:16:04
14 on how the parties behave with each other in terms of 12:16:08
15 exchange of information. 12:16:11

16 And then you have licensing negotiations, 12:16:13
17 and then you also have licensing -- you know, a 12:16:16
18 license or some other type of contract. But 12:16:19
19 there's -- that defines what the professional 12:16:22
20 relationship is. And so that's really what I'm trying 12:16:25
21 to find out, and so from what I've -- so I'll just -- 12:16:27
22 that's for context; it's not a question. 12:16:32

23 So my understanding is, based on your 12:16:36
24 testimony and then these documents, is that [REDACTED] and 12:16:39
25 [REDACTED] began discussions of a potential licensing 12:16:45

1 arrangement for [REDACTED] starting around May of 12:16:56
2 2023; is that fair? 12:17:04

3 A May, yeah, that plus or minus a month, 12:17:08
4 something like that, yeah. 12:17:11

5 Q And then there was a CDA in place between 12:17:13
6 [REDACTED] and [REDACTED] during this time, to your 12:17:17
7 understanding? 12:17:20

8 A I've never seen it. I'm just assuming that 12:17:20
9 this would be the standard way that people operate. 12:17:23

10 Q Right. And then there's that email as well 12:17:26
11 where David Butler had said it had been entered? 12:17:29

12 A The CDA was in place with me, I didn't 12:17:33
13 know -- okay. Was that pertaining to [REDACTED] or 12:17:36
14 pertaining to me? 12:17:38

15 Q Yeah, that's a good -- yeah, so you're 12:17:39
16 right. So the CDA was in place with you -- 12:17:42

17 A Right. 12:17:45

18 Q Why was the CDA in place with you? Is that 12:17:45
19 because of the advisory board? 12:17:48

20 A No. He put the CDA in place with me even 12:17:50
21 before discussing it -- well, no. I think I have to 12:17:53
22 look at the emails, but it's just standard practice. 12:17:56
23 Any company I've ever dealt with, you can say hi, talk 12:17:59
24 about the weather. But if you want to talk anything 12:18:04
25 beyond the weather and something very, very light, you 12:18:07

1	got to do the CDA.	12:18:10
2	Q Right. Okay. So you're assuming that	12:18:12
3	there's a CDA between [REDACTED] and [REDACTED]	12:18:14
4	A That's my assumption.	12:18:19
5	Q Right. But you don't know for sure one way	12:18:20
6	or the other?	12:18:26
7	A I've never seen it.	12:18:26
8	Q But there were discussions about a potential	12:18:27
9	license that occurred between [REDACTED] and [REDACTED]	12:18:30
10	correct?	12:18:33
11	A Oh, they discussed that for sure.	12:18:33
12	Q What else -- what else besides that was	12:18:36
13	discussed between [REDACTED] and [REDACTED] in terms of a	12:18:42
14	professional relationship?	12:18:46
15	A I don't know. You would have to depose [REDACTED]	12:18:47
16	[REDACTED] All I know is general like bullet points. I	12:18:50
17	don't know really. I just know broad strokes of where	12:18:58
18	things are. And I think -- I'm not aware of any	12:19:03
19	contract that involves financial discussion --	12:19:06
20	financials at all between [REDACTED] and [REDACTED]	12:19:13
21	Q So your testimony is, sitting here today,	12:19:16
22	that you're not aware of a contract being executed	12:19:19
23	relating to [REDACTED] between [REDACTED] and [REDACTED]	12:19:25
24	right?	12:19:31
25	A Correct.	12:19:31

1	Q Are you aware whether discussions are	12:19:35
2	ongoing relating to a potential agreement between	12:19:39
3	[REDACTED] and [REDACTED] concerning [REDACTED]?	12:19:45
4	A To my knowledge, no. I think the way it --	12:19:47
5	again, I think the way it rectified itself was they	12:19:49
6	just are going to work directly with [REDACTED]	12:19:54
7	Q But you're saying that, but I just -- do you	12:19:56
8	know that for certain?	12:19:59
9	A Let me try to search my emails here. I	12:20:01
10	mean, I can just text [REDACTED] and find out. But just	12:20:08
11	give me a second, let me see if I can find an email	12:20:16
12	that says what the latest status is of this.	12:20:19
13	Okay. Here's the latest from the 13 --	12:22:24
14	February 13, one week ago. Minutes from the last	12:22:28
15	advisory board meeting. Discussions around -- here we	12:22:31
16	go. [REDACTED] has a [REDACTED] from [REDACTED] and we are	12:22:34
17	looking to [REDACTED]. That's it.	12:22:38
18	That's the current state of affairs as of one week	12:22:42
19	ago.	12:22:46
20	Q And when you say "we," that's Hongene?	12:22:46
21	A Yes.	12:22:49
22	Q Okay. That's coming from David Butler?	12:22:53
23	A That is the meeting minutes from David	12:22:55
24	Butler from the February 13 meeting.	12:22:57
25	MR. SHORES: Okay. We're going to need a	12:23:03

1	copy of that, Jeremy. We didn't have that.	12:23:04
2	MR. EDWARDS: Like I said, please compile	12:23:16
3	your requests into a letter --	12:23:19
4	MR. SHORES: I can put it into the record,	12:23:21
5	too, which is what I'm doing. So -- and I will do	12:23:22
6	that, I will send you a list as well, but I'm entitled	12:23:27
7	to put it in the record.	12:23:31
8	Q Okay. In terms of -- is [REDACTED] involved in	12:23:43
9	any other discussions with [REDACTED] concerning any	12:23:53
10	other professional relationship?	12:24:01
11	A I think they're also looking into the	12:24:04
12	right -- evaluating different [REDACTED] on the [REDACTED]	12:24:09
13	[REDACTED] that work best with [REDACTED].	12:24:12
14	Q And what is that -- is that under an	12:24:16
15	agreement or are they just discussions, or what are	12:24:24
16	we --	12:24:28
17	A I think it's just [REDACTED]. So I	12:24:29
18	think [REDACTED] is [REDACTED] to [REDACTED] and [REDACTED]	12:24:32
19	is taking a look and doing some things on their	12:24:37
20	[REDACTED] and [REDACTED]. I don't think there's	12:24:42
21	any money involved at all. It's just [REDACTED]	12:24:43
22	[REDACTED] and [REDACTED] and [REDACTED]	12:24:46
23	[REDACTED]. It's all friendly.	12:24:50
24	Q What about other collaborative efforts	12:24:54
25	between [REDACTED] and [REDACTED] is that it or are there any	12:24:57

1	more?	12:25:02
2	A That's all I'm aware of is [REDACTED]	12:25:02
3	[REDACTED], a [REDACTED],	12:25:05
4	which [REDACTED] is good, that's it.	12:25:10
5	Q So in your January 22nd, 2024 deposition, I	12:26:05
6	asked you whether Elsie would consider licensing P(V)	12:26:13
7	to Hongene.	12:26:19
8	Do you recall that?	12:26:20
9	A I -- you can go ahead and tell me what I	12:26:21
10	said. I don't recall. I'm sure they would consider	12:26:24
11	that. They would have.	12:26:27
12	Q Well, you didn't respond affirmatively. You	12:26:29
13	testified that "I don't think they legally can."	12:26:32
14	A Exactly, which is why they're now working	12:26:35
15	with [REDACTED]	12:26:37
16	Q Right. But you -- you agreed to provide	12:26:39
17	full, complete, and truthful testimony and didn't	12:26:51
18	you -- why didn't you disclose that?	12:26:57
19	A Disclose what?	12:26:59
20	Q Why didn't you disclose these discussions	12:27:01
21	that were happening between [REDACTED] and [REDACTED]	12:27:09
22	A I think I did and I didn't leave anything	12:27:12
23	off the table. I told you very clearly that Aldrich	12:27:16
24	or Millipore-Sigma has the rights to sell it as a	12:27:20
25	reagent. [REDACTED] did not -- they were trying to get it,	12:27:23

1 and I think the conclusion as of a couple of weeks ago 12:27:26
2 was that they can't get that part and so [REDACTED] will 12:27:30
3 just work directly with [REDACTED]. 12:27:34

4 What's -- what's not disclosed? 12:27:36

5 Q Well, you didn't disclose any of these 12:27:38
6 relationships, the discussions between [REDACTED] and 12:27:44

7 [REDACTED] You didn't -- you didn't disclose any of 12:27:47
8 that in any of your declarations or in your -- in your 12:27:51
9 deposition. 12:27:55

10 MR. EDWARDS: Ask a question. 12:27:56

11 Q Is that correct? 12:27:59

12 A I also didn't disclose, you know, my 12:28:00
13 favorite color sweater, my kids' sports that they go 12:28:04
14 into. 12:28:11

15 This is so irrelevant to the case, I think 12:28:11
16 it's sad. I feel sorry for your client that this is 12:28:13
17 what you're doing. It's irrelevant. Why would I put 12:28:18
18 that in the declaration? It's irrelevant. None of 12:28:20
19 this is relevant to the case. 12:28:23

20 I'm sorry your client is paying for this. I 12:28:25
21 know you'll strike it from the record. Go ahead. 12:28:29

22 THE VIDEOGRAPHER: I'm sorry, Counsel, this 12:28:51
23 is the videographer, I only have 10 minutes left on my 12:28:52
24 tape. 12:28:56

25 MR. SHORES: Okay. We'll come up to a 12:28:56

1	stopping point shortly.	12:28:59
2	BY MR. SHORES:	12:29:03
3	Q And, Dr. Baran, do you recall I also during	12:29:03
4	your -- your deposition, I also asked you whether	12:29:07
5	Elsie had a contract with Hongene and you said no.	12:29:10
6	Do you remember that?	12:29:15
7	A I still don't know if they have a contract.	12:29:17
8	I just assumed they might have a CDA in place.	12:29:20
9	Q But your testimony is you didn't feel the	12:29:24
10	need to disclose those -- these discussions that we	12:29:27
11	covered in this -- recently in this deposition, right?	12:29:30
12	MR. EDWARDS: Object to form. Vague.	12:29:32
13	A Again, I don't know what discussions you're	12:29:36
14	talking about. What -- I guess my feeling back in	12:29:38
15	January was I was surprised by the number of hours you	12:29:41
16	spent on things which have nothing to do with this	12:29:46
17	case. I mean, I'm getting paid either way so I'll	12:29:50
18	talk all day about whatever you want, give you a	12:29:54
19	lecture on organic chemistry or talk about plastic	12:29:58
20	bottles, whatever you like.	12:30:02
21	So if I didn't disclose something, it's not	12:30:03
22	because I was trying to withhold it. It's because not	12:30:05
23	in my wildest imagination would I think it was at all	12:30:07
24	even relevant.	12:30:12
25	But you ask whatever you want. You have	12:30:13

1	whatever emails you want.	12:30:13
2	I state for the record I have absolutely	12:30:15
3	nothing to hide here. So just ask what you want,	12:30:17
4	you'll get whatever you want. I'll show you my	12:30:20
5	emails, I'll screen share whatever you would like,	12:30:23
6	sir. There's nothing to hide.	12:30:27
7	MR. SHORES: I think it's probably a good	12:30:41
8	stopping point here. We can break for lunch.	12:30:43
9	MR. EDWARDS: Yeah, that's fine with me here	12:30:52
10	on the East Coast.	12:30:55
11	THE VIDEOGRAPHER: All right. We are going	12:30:57
12	off the record at 12:31 p.m.	12:30:59
13	(Recess 12:31 p.m. - 12:43 p.m.)	12:31:03
14	THE VIDEOGRAPHER: We are going back on the	12:43:33
15	record at 12:43 p.m.	12:43:40
16	MR. SHORES: Okay. If we can pull up	12:43:43
17	Exhibit 1003, please.	12:43:45
18	THE TECHNICIAN: Counsel, you said 1003,	12:43:58
19	correct?	12:44:02
20	MR. SHORES: Yeah, thank you. Actually, can	12:44:06
21	you pull up instead Exhibit 2036.	12:44:47
22	THE TECHNICIAN: Yes, stand by.	12:44:56
23	It's on screen.	12:45:03
24	BY MR. SHORES:	12:45:11
25	Q And, Dr. Baran, on Exhibit 2036, the email	12:45:11

1	from David Butler to you dated May 17, 2023 states, "I	12:45:14
2	am curious whether your involvement with AsymChem	12:45:22
3	represents a possible COI as they are a competitor of	12:45:22
4	Hongene around oligonucleotides and raw materials for	12:45:27
5	manufacturing them."	12:45:31
6	Did I read that correctly?	12:45:33
7	A Yes.	12:45:35
8	Q And if we move up in this document to the	12:45:35
9	top of the page.	12:45:39
10	A I'm trying.	12:45:47
11	Q That's fine. And then that email -- the	12:45:48
12	email from you to David Butler and Michelle Gassert	12:45:52
13	states, "Not an issue. AsymChem officially ended	12:45:57
14	their SAB so I'm no longer working with them."	12:46:01
15	Do you see that?	12:46:05
16	A Yes.	12:46:06
17	Q When did that end? When did the AsymChem	12:46:06
18	SAB service end?	12:46:14
19	A The entire SAB was disbanded. They just	12:46:15
20	don't do it anymore. I believe 2022 was the last	12:46:20
21	year.	12:46:25
22	Q Okay. As like you were saying earlier,	12:46:26
23	that, you know, sometimes these SABs pop up, sometimes	12:46:31
24	they go away?	12:46:36
25	A Yeah. Exactly.	12:46:37

1	Q	So sitting here today, you don't have that	12:46:38
2	--	you're not on their advisory board because it	12:46:42
3		doesn't exist, correct?	12:46:48
4	A	No. And as an aside, I never in any	12:46:49
5		capacity worked with them on oligonucleotides.	12:46:53
6	Q	Okay. All right. If we can pull up Exhibit	12:46:55
7		1003, please. And if we can go to -- it's your CV and	12:47:00
8		so it will be page 81 legended on the bottom.	12:47:20
9		And then under the heading of "Editorial	12:47:40
10		Activities and Advisory Boards," do you see that?	12:47:46
11	A	Yes.	12:47:49
12	Q	So you identified AsymChem there, correct --	12:47:50
13		or did you?	12:47:58
14	A	I don't see it there. These are more for	12:48:00
15		journals.	12:48:04
16	Q	Okay. Okay. For some reason I thought you	12:48:05
17		had done that. But in any event, you list advisory	12:48:16
18		board participation here in your CV, correct?	12:48:24
19	A	Yeah. This was for -- for journals.	12:48:28
20	Q	For journals. Okay. I'm sorry. If you go	12:48:32
21		to the next page, 82, and you see that there are	12:48:37
22		scientific advisory boards listed there, I guess, for	12:48:53
23		-- with companies.	12:48:56
24		Do you see that?	12:48:58
25	A	Yeah.	12:48:59

1	Q	And you list a number of companies there	12:49:00
2		where you serve on their scientific advisory board?	12:49:04
3	A	Yeah.	12:49:08
4	Q	So you testified earlier you didn't think it	12:49:09
5		was relevant to disclose your service on Hongene's	12:49:18
6		advisory board. But here you disclosed your service	12:49:22
7		on other advisory boards, right?	12:49:27
8	A	Well --	12:49:29
9		MR. EDWARDS: Object to form.	12:49:30
10		Go ahead.	12:49:31
11	A	It's not that I didn't feel I needed to	12:49:32
12		represent. I didn't even look at my CV. Shelly	12:49:35
13		handles my CV. It's, you know, quite long. And	12:49:39
14		there's things on here -- I have to tell Shelly to	12:49:42
15		update it, because Kemxtree is outdated, AsymChem is	12:49:45
16		outdated, Nutcracker is not on here. There's other	12:49:51
17		ones that are not on here. Hongene needs to be added.	12:49:55
18		I believe that the CV doesn't even have --	12:49:59
19		yeah, it doesn't even have my current title. That's	12:50:01
20		not even my title anymore. So I just need to tell	12:50:04
21		Shelly to update that and get you the updated CV.	12:50:07
22		It's, you know, my fault because I thought Shelly has	12:50:10
23		a running tab update. But the CV changes quite often.	12:50:13
24		So every month it's different because publications are	12:50:18
25		added, patents are added, different consulting	12:50:21

1	relationships.	12:50:24
2	So you can put that in your to-do list for	12:50:24
3	Jeremy. We need to send you a like radically updated	12:50:28
4	CV that has everything as of today.	12:50:32
5	Q Yeah. Okay. Then having your updated CV	12:50:37
6	would be, you know, would be helpful.	12:50:43
7	A For sure.	12:50:46
8	MR. SHORES: So if we can go to Exhibit	12:50:49
9	2032.	12:50:54
10	THE TECHNICIAN: Stand by.	12:50:56
11	(Baran Exhibit 2032 marked for	12:50:57
12	identification.)	12:51:18
13	Q And, Dr. Baran, do you see this Exhibit	12:51:18
14	2032?	12:51:23
15	A Yeah.	12:51:23
16	Q And have you seen this document before?	12:51:24
17	A Yeah.	12:51:26
18	Q And what is this document?	12:51:26
19	A It's the deposition transcript from January.	12:51:29
20	Q Okay. And if we can go to page 85 of this	12:51:34
21	exhibit -- page 85 of the transcript -- yeah. Oh,	12:51:43
22	that was fast. Okay.	12:51:49
23	And if you scroll down to line 16, there it	12:51:53
24	says:	12:51:59
25	"QUESTION: And how many shares do you own	12:52:00

1	in Elsie?"	12:52:02
2	And your answer was: "Oh, I don't know the	12:52:04
3	number of shares. It's around, I think, around	12:52:07
4	3 million or so.	12:52:10
5	"QUESTION: And what percentage of ownership	12:52:11
6	do you have in Elsie?"	12:52:13
7	And you testified: "I think it's about 10	12:52:15
8	percent."	12:52:17
9	Did I read that correctly?	12:52:19
10	A Yeah.	12:52:20
11	Q So is that -- sitting here today, is that	12:52:21
12	still accurate?	12:52:23
13	A Yeah. I mean, I can go to the Carta app and	12:52:24
14	give you the exact number. Do you want me to do that?	12:52:27
15	Q I don't think that's necessary.	12:52:30
16	A Okay.	12:52:32
17	MR. SHORES: Okay. So I don't have any	12:52:36
18	further questions at this time.	12:52:37
19	MR. EDWARDS: I got a couple.	12:52:44
20	EXAMINATION	12:52:47
21	BY MR. EDWARDS:	12:52:47
22	Q Dr. Baran, can you hear me?	12:52:48
23	A Yeah.	12:52:50
24	Q At any point did you intentionally withhold	12:52:50
25	information about your service on Hongene's scientific	12:52:53

1	advisory board in this matter?	12:52:57
2	A No.	12:52:58
3	Q How about your relationship with Elsie?	12:52:58
4	A No.	12:53:01
5	Q How about [REDACTED] relationship and dealings	12:53:01
6	with [REDACTED]	12:53:04
7	A No.	12:53:06
8	Q What effect, if any, do any of those	12:53:08
9	relationships have on your analysis of the scientific	12:53:12
10	issues in this case?	12:53:15
11	A Absolutely zero.	12:53:15
12	(This concludes the confidential portion.)	12:53:17
13	MR. EDWARDS: No more questions.	12:53:17
14	MR. SHORES: No more questions.	12:53:20
15	MR. EDWARDS: Just to be clear, this	12:53:24
16	transcript needs to be marked as attorneys' eyes only,	12:53:26
17	confidential under the Protective Order and treated	12:53:30
18	accordingly.	12:53:33
19	THE VIDEOGRAPHER: Let me take us off the	12:53:43
20	record.	12:53:44
21	This marks the end of the continued	12:53:45
22	deposition of Phil Baran, M.D. [sic]. We are going	12:53:47
23	off of the record at 12:53 p.m.	12:53:51
24	(Time noted: 12:53 p.m.)	
25		

CERTIFICATE OF CERTIFIED SHORTHAND REPORTER
NOTARY PUBLIC

I, MONIQUE VOUTHOURIS, Certified Court
Reporter and Notary Public within and for the State of
New Jersey, do hereby certify:

That PHIL S. BARAN, PH.D., the witness whose
deposition is hereinbefore set forth, was duly sworn
by me before the commencement of such deposition, and
that such deposition was taken before me and is a true
record of the testimony given by such witness.

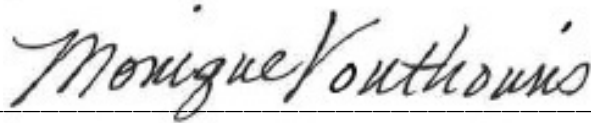
I further certify that the adverse party,
Shanghai Hongene Biotech, was represented by counsel
at the deposition.

I further certify that the deposition of
PHIL S. BARAN, PH.D. occurred remotely on Tuesday,
February 20, 2024, commencing at 8:02 a.m. EST to
12:53 p.m. EST.

I further certify that I am not related to
any of the parties to this action by blood or
marriage, I am not employed by or an attorney to any
of the parties to this action, and that I am in no way
interested, financially or otherwise, in the outcome
of this matter.

IN WITNESS WHEREOF, I have hereunto set my

1 hand this 21st day of February 2024.

2
3
4 
5

6 Monique Vouthouris, CCR, RPR, CRR

7 Notary Public of the State of New Jersey

8 My commission expires: April 8, 2024

A			
a-year	133:24, 135:17,	acetylated	addressed
122:8	136:7, 137:10,	65:16	94:23
ability	144:1, 144:3,	achieve	adds
19:25, 53:2,	144:25, 146:24,	113:11	22:20
125:22, 132:21,	147:8, 149:24,	achieved	adenosine
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able	158:25, 159:3,	49:1	21:20, 137:21
13:6, 17:11,	159:5	acidic	administrative
21:16, 66:22,	absolutely	59:8	107:25
67:21, 87:17,	153:2, 159:11	acids	advance
87:19, 92:10,	ac	7:4	32:10, 34:9,
129:25, 136:22	65:17, 67:5	act	108:11
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16:3, 17:10,	84:24, 132:13,	action	136:22
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