

EXHIBIT A

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA

THE BOARD OF TRUSTEES OF THE
LELAND STANFORD JUNIOR
UNIVERSITY,

Plaintiff,

vs.

No. C-05-04158-MHP

ROCHE MOLECULAR SYSTEMS, INC,
et al.,

Defendants.

CERTIFIED
COPY

AND RELATED COUNTERCLAIM.

DEPOSITION OF PAUL VOLBERDING, M.D.

Palo Alto, California

Sunday, August 19, 2007

Reported by:
GINA GLANTZ
CSR No. 9795, RPR, RMR

JOB No. 3-70580

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UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA

THE BOARD OF TRUSTEES OF THE
LELAND STANFORD JUNIOR
UNIVERSITY,

Plaintiff,

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No. C-05-04158-MHP

ROCHE MOLECULAR SYSTEMS, INC,
et al.,

Defendants.

AND RELATED COUNTERCLAIM.

Deposition of PAUL VOLBERDING, M.D., taken
on behalf of Roche Defendants, at 3000 El Camino Real,
Five Palo Alto Square, 4th Floor, Palo Alto, California,
beginning at 10:10 a.m. and ending at 3:40 p.m., on
Sunday, August 19, 2007, before GINA GLANTZ, Certified
Shorthand Reporter No. 9795.

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11:39:13 1 MS. RHYU: Objection. Vague as to time, vague
11:39:16 2 as to "therapy."

11:39:19 3 THE WITNESS: Patients can receive medications
11:39:23 4 through conventional prescriptions or through
11:39:27 5 participating in clinical investigations.

11:39:33 6 BY MR. CANNON:

11:39:34 7 Q So in 1991 when this article was published, is
11:39:41 8 it true that the only way for an HIV-infected patient to
11:39:45 9 obtain an antiretroviral therapy other than zidovudine
11:39:52 10 was to be enrolled in a clinical trial?

11:39:55 11 A When this article was published, which was,
11:40:00 12 again, in January, it looks to be, 1991, zidovudine was
11:40:05 13 the only prescription antiretroviral available, yes.

11:40:12 14 Q In 1991, do you know what percentage of
11:40:16 15 HIV-infected patients were enrolled in clinical trials?

11:40:22 16 MS. RHYU: Objection. Calls for speculation.

11:40:32 17 THE WITNESS: I don't have any knowledge of how
11:40:34 18 many patients were involved in clinical trials in 1991.

11:40:44 19 BY MR. CANNON:

11:40:44 20 Q Is it fair to say that in 1991 the majority of
11:40:49 21 patients who suffered from HIV infection were not
11:40:52 22 receiving therapy -- antiretroviral therapy, other than
11:40:57 23 zidovudine?

11:40:58 24 MS. RHYU: Objection. Calls for speculation,
11:41:00 25 lacks foundation.

11:52:23 1 1995, but I'm referring here to the one in early 1996,
11:52:28 2 yes.

11:52:28 3 Q So did clinical investigators -- strike that.

11:52:33 4 Is it true that clinical investigators were not
11:52:38 5 aware of the results of these trials until they were
11:52:40 6 unveiled in 1995 and early 1996?

11:52:43 7 MS. RHYU: Objection. Lacks foundation, calls
11:52:45 8 for speculation.

11:52:46 9 THE WITNESS: I believe the earliest
11:52:49 10 presentations of data from the trials were in 1995.

11:52:54 11 BY MR. CANNON:

11:52:55 12 Q Was that at the Vancouver AIDS Conference?

11:52:58 13 A No, that was later, in 1996.

11:53:00 14 Q Do you know, was there a particular conference
11:53:03 15 you have in mind for the 1995 presentation of data?

11:53:06 16 A I don't recall which specific conference was --
11:53:09 17 the data were presented in 1995.

11:53:11 18 Q But you're sure that 1995 is the year that the
11:53:16 19 data was presented?

11:53:18 20 A Yes, I'm sure.

11:53:19 21 Q Is there a particular reason why you're sure
11:53:22 22 about that date?

11:53:23 23 A Only because I've been corrected in my earlier
11:53:29 24 assumption that it was presented for the first time in
11:53:33 25 January of 1996.

11:53:35 1 Q Were you at the conference at which the first
11:53:38 2 presentation of the data occurred?

11:53:40 3 A I was present at the conference in January
11:53:43 4 1996, when I saw the data for the first time.

11:53:48 5 Q And that was the data from a trial involving a
11:53:51 6 combination of three different antiretroviral therapies?

11:53:55 7 A Yes, that's right.

11:53:56 8 Q And one of them was indinavir?

11:54:00 9 A That's correct.

11:54:01 10 Q Was that the first presentation of a trial
11:54:05 11 involving a protease inhibitor?

11:54:09 12 MS. RHYU: Objection. Calls for speculation,
11:54:11 13 lacks foundation.

11:54:11 14 THE WITNESS: Again, I believe that data from
11:54:18 15 protease trials were presented in 1995, but this was the
11:54:28 16 first presentation of data using a protease and two
11:54:33 17 other drugs that I heard presented publicly.

11:54:38 18 BY MR. CANNON:

11:54:42 19 Q And participants in the conference or the
11:54:45 20 conferences in 1995 and 1996, when this data was
11:54:49 21 presented, they would include those of ordinary skill in
11:54:51 22 the art, as you've defined it, in connection with these
11:54:54 23 patents; correct?

11:54:58 24 A Well, the --

11:54:59 25 MS. RHYU: Objection. Compound, calls for

12:30:21 1 get sent?

12:30:23 2 MS. RHYU: Objection. Outside the scope.

12:30:24 3 THE WITNESS: Of course.

12:30:26 4 BY MR. CANNON:

12:30:29 5 Q When you get the results back, does the lab
12:30:31 6 make recommendations about the therapy for a particular
12:30:33 7 patient?

12:30:34 8 MS. RHYU: Objection. Outside the scope. Can
12:30:45 9 you identify what claim construction term your question
12:30:48 10 relates to, Brian?

12:30:52 11 MR. CANNON: All of my questions today relate
12:30:53 12 to "therapeutically effective" and the remainder of the
12:30:56 13 claim terms at issue.

12:31:06 14 MS. RHYU: I don't see how that question that
12:31:08 15 you posed regarding lab recommendations today relate to
12:31:16 16 construction of the claim term "therapeutically
12:31:19 17 effective." Can you make a connection there?

12:31:22 18 MR. CANNON: Well, then you can instruct him
12:31:24 19 not to answer. I don't need to lay out for you where
12:31:26 20 I'm going or what my strategy is.

12:31:27 21 MS. RHYU: Okay. Then I instruct the witness
12:31:29 22 not to answer.

12:31:29 23 (Instruction not to answer.)

12:31:29 24 MR. CANNON: Could you repeat my question back
12:31:31 25 so we get the instruction clearly?

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(Record read.)

MS. RHYU: I instruct the witness not to answer because it's outside the scope of claim construction testimony.

BY MR. CANNON:

Q Dr. Volberding, when you get the results back from the lab, does the manufacturer of the test kit make recommendations about a patient's therapy?

MS. RHYU: Same instruction.

(Instruction not to answer.)

BY MR. CANNON:

Q When you get the results back from the lab, Dr. Volberding, does the manufacturer of the test kit make a determination about the effectiveness of the therapy for the particular patient?

MS. RHYU: Same objection.

BY MR. CANNON:

Q The treating physician makes a decision --

MS. RHYU: And instruction, sorry.

(Instruction not to answer.)

BY MR. CANNON:

Q And Dr. Volberding, do you follow your counsel's instructions with respect to answering the last few questions?

A Yes, I do.

12:35:19 1 THE WITNESS: I think, as I've said, the
12:35:22 2 physician has a central role in that determination, but
12:35:29 3 in fact, the information comes from a number of sources,
12:35:35 4 and many times the key information comes from someone
12:35:37 5 other than the physician.

12:35:38 6 BY MR. CANNON:

12:35:38 7 Q I understand that information may come from a
12:35:41 8 number of sources. I'm trying to pin down to see if
12:35:44 9 there is an answer for the question as to who makes the
12:35:47 10 ultimate conclusion, if anyone, about the effectiveness
12:35:50 11 of therapy for a particular patient.

12:35:53 12 A Well, and in terms of accepting responsibility
12:35:57 13 for the decision, I think many of the people on the team
12:36:00 14 that I just mentioned would share in that
12:36:03 15 responsibility. Certainly, again, I'm not saying the
12:36:06 16 physician doesn't have an important role in that.

12:36:10 17 Q But is it your testimony that the physician is
12:36:13 18 not the only person that makes the conclusion about the
12:36:16 19 effectiveness of therapy?

12:36:18 20 A That's correct.

12:36:18 21 Q Does the lab that performed the assay make a
12:36:30 22 conclusion about the effectiveness of therapy?

12:36:33 23 MS. RHYU: You're asking about that today?

12:36:35 24 MR. CANNON: Today.

12:36:35 25 MS. RHYU: I instruct the witness not to answer

12:36:38 1 as being outside the scope of this deposition.

12:36:39 2 (Instruction not to answer.)

12:36:39 3 BY MR. CANNON:

12:36:40 4 Q Do you follow counsel's instructions?

12:36:42 5 A Yes, I do.

12:36:43 6 Q Does the manufacturer of the test kit make a
12:36:47 7 conclusion about the effectiveness of therapy for a
12:36:51 8 particular patient?

12:36:52 9 MS. RHYU: Same instruction.

12:36:53 10 (Instruction not to answer.)

12:36:53 11 BY MR. CANNON:

12:36:54 12 Q Do you follow counsel's instruction?

12:36:55 13 A I do.

12:37:07 14 MR. CANNON: Now would be a good time to stop
12:37:09 15 for a break?

12:37:09 16 MS. RHYU: I'm not sure. Yes, why don't we
12:37:14 17 stop. I hear the elevator.

12:37:17 18 THE VIDEOGRAPHER: The time is 12:37. We're
12:37:18 19 going off the record.

13:24:03 20 (Lunch recess.)

13:26:59 21 THE VIDEOGRAPHER: Good afternoon. The time is
13:27:01 22 1:27. We are back on the record.

13:27:05 23 BY MR. CANNON:

13:27:05 24 Q Dr. Volberding, before the break we were
13:27:08 25 looking at Exhibit 11, which was an article from Nature

13:27:12 1 Medicine. If you could put that in front of you.

13:27:15 2 A Okay.

13:27:16 3 Q All right. On the first page, there -- on the
13:27:19 4 second column, there's a paragraph under the title
13:27:22 5 "Correlation of HIV RNA levels to stage of disease." Do
13:27:26 6 you see that?

13:27:26 7 A Yes, I do.

13:27:28 8 Q And the first sentence reads "Early studies
13:27:35 9 demonstrated a clear association between the titer of
13:27:37 10 culturable virus in the plasma and the clinical stage of
13:27:43 11 disease." Do you see that?

13:27:44 12 A Yes, I do.

13:27:45 13 Q And there's three citations, three end notes
13:27:49 14 cited that. And they're notations to references 4, 5,
13:27:53 15 and 14. If you could turn with me to the last page of
13:27:59 16 this article, and I'd like you to just agree with me
13:28:02 17 that reference 4 is an article by an author named Ho,
13:28:10 18 published in The New England Journal of Medicine in
13:28:13 19 1989; reference 5 is by the author of Coombs, et al.,
13:28:17 20 published in The New England Journal of Medicine, also
13:28:20 21 in 1989; and reference 14 is by Clark, et al., also
13:28:25 22 published in The New England Journal of Medicine but in
13:28:29 23 1991. Do you see that?

13:28:30 24 A I do.

13:28:30 25 Q So each of the three articles that are cited in

13:28:36 1 support of the sentence on the first page of this
13:28:39 2 article were published in '89, '89, and '91
13:28:44 3 respectively. You would agree, then, would you not,
13:28:47 4 that before 1992, early studies demonstrated a clear
13:28:53 5 association between the titer of culturable virus in the
13:28:58 6 plasma and the clinical stage of disease?

13:29:13 7 MS. RHYU: Objection. Document speaks for
13:29:17 8 itself.

13:29:18 9 THE WITNESS: It's not an area that I reviewed
13:29:28 10 in detail for the deposition today, but I agree that
13:29:32 11 that's what this article refers to, sure.

13:29:38 12 BY MR. CANNON:

13:29:53 13 Q Do you believe -- do you believe that
13:30:00 14 Drs. Holodniy, Merigan and Katzenstein were the first to
13:30:02 15 establish the association between viral load and
13:30:04 16 clinical stage of the disease?

13:30:07 17 MS. RHYU: Objection. Outside the scope. If
13:30:11 18 you -- and lacks foundation.

13:30:14 19 Dr. Volberding, if you feel that you can answer
13:30:17 20 based on any review that you've done, please go ahead.

13:30:26 21 THE WITNESS: You know, I'm not expecting to
13:30:31 22 render an opinion as to -- as to whether they were the
13:30:40 23 first to show an association, as you've said in your
13:30:44 24 question.

13:30:44 25 BY MR. CANNON:

14:16:44 1 statistically. It's unusual for a specific test in a
14:16:52 2 specific patient to be analyzed statistically.

14:16:55 3 BY MR. CANNON:

14:17:01 4 Q So is it your testimony -- and correct me if
14:17:04 5 I'm misstating this in any way. Is it your testimony
14:17:08 6 that, as of May 1992, one of skill in the art would not
14:17:12 7 consider it -- a treating physician to be the person
14:17:20 8 that evaluates whether or not a statistically
14:17:23 9 significant decline has taken place?

14:17:37 10 MS. RHYU: Same objections. Outside the scope,
14:17:39 11 lacks foundation.

14:17:44 12 THE WITNESS: My assumption would be that the
14:17:48 13 physician might compare a result against the performance
14:17:56 14 of a test, and that the statistical significance would
14:18:03 15 have been established in other settings.

14:18:04 16 BY MR. CANNON:

14:18:04 17 Q So the statistical significance is not the data
14:18:11 18 for a particular patient, but that patient as compared
14:18:16 19 to a number of patients that have gone previously?

14:18:20 20 A I think, in general, the statistical
14:18:23 21 significance would have been generated from data from
14:18:26 22 larger groups of patients, not a specific patient under
14:18:29 23 treatment.

14:18:29 24 Q In May 1992, how much of a decline in HIV RNA
14:18:44 25 copy number would be considered statistically

14:18:47 1 significant by those with skill in the art?

14:18:49 2 A I haven't --

14:18:53 3 MS. RHYU: Hold on just a sec.

14:19:14 4 Objection. Lacks foundation, assumes facts not
14:19:18 5 in evidence.

14:19:19 6 Go ahead.

14:19:19 7 THE WITNESS: Yeah, it's not an area that I
14:19:21 8 reviewed specifically for the deposition. I assume that
14:19:28 9 data is very available, but I couldn't, as I sit here,
14:19:34 10 give you the exact numbers.

14:19:36 11 BY MR. CANNON:

14:19:36 12 Q But you offered an opinion about the meaning of
14:19:39 13 the phrase "statistically significant decline"; right?

14:19:42 14 A Yes, I did.

14:19:43 15 Q Just so I've got the testimony fully clear, but
14:19:47 16 you don't have an opinion as to how much of a decline
14:19:49 17 was statistically significant as of May 1992?

14:19:53 18 A If I could have you refer back to my
14:19:57 19 declaration --

14:19:57 20 Q Sure.

14:19:57 21 A -- so I could look at that section.

14:20:00 22 Q Absolutely. Absolutely. And if you need to
14:20:03 23 take a little time to read it to answer the question,
14:20:06 24 please do.

14:20:20 25 MS. RHYU: And I'll object to that pending

14:20:22 1 question as misstating the prior testimony and
14:20:28 2 mischaracterizing that declaration.

14:20:34 3 THE WITNESS: So --

14:20:34 4 MS. RHYU: Also misleading.

14:20:36 5 THE WITNESS: -- I'm waiting to be directed
14:20:38 6 where you're referring in my declaration.

14:20:41 7 BY MR. CANNON:

14:20:41 8 Q No, I was asking -- I was looking at paragraph
14:20:43 9 17 of your declaration, which is the paragraph that I
14:20:47 10 understood in which you rendered your opinions about
14:20:55 11 statistically significant decline. And so please feel
14:21:02 12 free to read that paragraph or any of the other
14:21:02 13 paragraphs in the dec.

14:21:04 14 A Okay.

14:21:04 15 MR. CANNON: And could we go back, Gina, to, I
14:21:06 16 think, two questions ago, where I had a question that
14:21:10 17 prompted going to the dec.

14:21:34 18 (Record read as follows:

14:21:34 19 "Q Just so I've got the testimony
14:21:34 20 fully clear, but you don't have an
14:21:34 21 opinion as to how much of a decline was
14:21:34 22 statistically significant as of May
14:21:35 23 1992?")

14:21:35 24 MS. RHYU: Same objections and vague. Are you
14:21:37 25 asking him what statistically significant means?

14:21:42 1 MR. CANNON: I'm just asking him the question.

14:21:44 2 Q Can you answer it?

14:21:44 3 A My reading of my declaration, I think it's
14:21:48 4 clear that I was referring to a general understanding of
14:21:55 5 what statistical significance is, not to a specific
14:21:57 6 number of decline in viral load.

14:21:59 7 Q Would one of skill in the art in 1992 have had
14:22:04 8 an understanding as to how much of a decline was
14:22:10 9 statistically significant?

14:22:12 10 MS. RHYU: Asked and answered.

14:22:13 11 THE WITNESS: My belief is that a person of
14:22:15 12 skill in the art in 1992 would understand what the term
14:22:19 13 "statistically significant" meant, and would refer to
14:22:25 14 published numbers in publications or package inserts or
14:22:33 15 some other source to know what the specific numbers
14:22:36 16 were.

14:22:37 17 BY MR. CANNON:

14:22:37 18 Q What publications or package inserts were
14:22:41 19 available to those of skill in the art in May 1992 to
14:22:45 20 make that determination?

14:22:47 21 MS. RHYU: Objection. Lacks foundation, vague.

14:22:51 22 THE WITNESS: I'm -- I didn't review all of the
14:22:54 23 publications that might have been available, but
14:22:57 24 certainly some of them are ones that have been discussed
14:23:02 25 in the context of this -- of these claims.

14:23:03 1 BY MR. CANNON:

14:23:04 2 Q Right, we -- but were those available in May
14:23:08 3 1992?

14:23:10 4 MS. RHYU: Objection. Vague. Again, are you
14:23:13 5 asking him to define what statistically significant is?

14:23:18 6 THE WITNESS: I don't know, as I sit here, all
14:23:20 7 of the publications that would have analyzed the
14:23:26 8 significance of declines in numbers of viral load in May
14:23:30 9 of 1992.

14:23:31 10 BY MR. CANNON:

14:23:31 11 Q Can you identify any publications that would
14:23:35 12 provide information to those of skill in the art that
14:23:38 13 would allow them to determine whether a particular
14:23:41 14 decline was statistically significant?

14:23:44 15 MS. RHYU: Objection. Lacks foundation,
14:23:46 16 misleading to suggest that statistically significant
14:23:51 17 requires a particular number.

14:23:57 18 THE WITNESS: Could you repeat your question?

14:23:59 19 MR. CANNON: Could you read it back, please.

14:24:13 20 (Record read.)

14:24:24 21 THE WITNESS: In 1992 --

14:24:26 22 MS. RHYU: Same objections.

14:24:27 23 THE WITNESS: -- clinicians, were they to
14:24:38 24 perform viral load testing, would likely have referred
14:24:41 25 to the research papers that have been included in this

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patent.

BY MR. CANNON:

Q Can you give me a specific example, sitting here today, of any of those papers?

A I'd have to look at the literature to find specific papers. I wasn't expecting to be able to cite articles that gave specific numbers like that.

Q So the answer is, without further research that you might undertake, you can't -- you can't provide a specific citation sitting here today?

MS. RHYU: Objection. Misstates prior testimony, misleading, lacks foundation.

THE WITNESS: I said that I was --

MS. RHYU: And he -- and he can answer questions as to the meaning of statistical significance.

THE WITNESS: I said that I was prepared to talk about the definition of statistical significance, but wasn't expecting to identify exact references or numbers.

BY MR. CANNON:

Q Right, I understand that. I'm just trying to close out the testimony so we're all on the same page.

So sitting here today, you cannot identify a particular reference or publication at or before May 1992 that would provide the data that we've been

14:26:04 1 discussing; correct?

14:26:05 2 MS. RHYU: Objection. Vague.

14:26:05 3 THE WITNESS: I haven't had a chance to review

14:26:07 4 the literature to answer that question.

14:26:14 5 BY MR. CANNON:

14:26:14 6 Q Looking back at the claims of the '705

14:26:20 7 patent --

14:26:22 8 A Okay.

14:26:23 9 Q -- and let's look at claims 6 and 7. Did you

14:26:27 10 review those claims?

14:26:29 11 A Yes, I did.

14:26:29 12 Q And claim 6 uses the phrase "statistically

14:26:36 13 significant decline"; correct?

14:26:38 14 A Yes, it does.

14:26:39 15 Q And that's a phrase that you've provided an

14:26:42 16 opinion for; correct?

14:26:42 17 A That's correct.

14:26:43 18 Q And let me just read claim 6. "The method of

14:26:48 19 claim 1 wherein the presence of a statistically

14:26:51 20 significant decline in plasma HIV RNA copy number

14:26:56 21 correlates positively that the antiretroviral agent is

14:27:00 22 therapeutically effective." Do you see that?

14:27:03 23 A Yes, I do.

14:27:03 24 Q Do you understand there to be a typo in that

14:27:15 25 claim or a mistake?