

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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BeiGene USA, Inc. and BeiGene, LTD.,

Petitioners,

v.

Pharmacyclics LLC

Patent Owner.

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PGR2024-00009

U.S. PATENT NO. 11,672,803

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| <div>1 Deposition via Zoom of DAVID A. SCOTT, a</div> <div>2 witness herein, called for examination by counsel for</div> <div>3 Petitioner in the above-entitled matter, pursuant to</div> <div>4 notice, the witness being duly sworn by MARY GRACE</div> <div>5 CASTLEBERRY, a Notary Public in and for the State of</div> <div>6 Maryland, taken at 8:43 a.m. EDT, Friday, September</div> <div>7 27, 2024, and the proceedings being taken down by</div> <div>8 Stenotype by MARY GRACE CASTLEBERRY, RPR, and</div> <div>9 transcribed under her direction.</div> <div>10</div> <div>11</div> <div>12</div> <div>13</div> <div>14</div> <div>15</div> <div>16</div> <div>17</div> <div>18</div> <div>19</div> <div>20</div> <div>21</div> <div>22</div> | Page 2 | <div>1 APPEARANCES (Continued):</div> <div>2</div> <div>3 On behalf of the Patent Owner:</div> <div>4 BRENDA L. DANEK, ESQ.</div> <div>5 Latham &amp; Watkins LLP</div> <div>6 330 North Wabash Avenue, Suite 2800</div> <div>7 Chicago, Illinois 60611</div> <div>8 (312) 876-7646</div> <div>9 brenda.danek@lw.com</div> <div>10</div> <div>11 ALSO PRESENT:</div> <div>12 DEWEY NELSON, Videographer</div> <div>13</div> <div>14</div> <div>15</div> <div>16</div> <div>17</div> <div>18</div> <div>19</div> <div>20</div> <div>21</div> <div>22</div>                                                                                                                                                                                                                                                                                                                                                     | Page 4 |
| <div>1 APPEARANCES:</div> <div>2</div> <div>3 On behalf of the Petitioner:</div> <div>4 PRIYATA Y. PATEL, ESQ.</div> <div>5 Weil, Gotshal &amp; Manges LLP</div> <div>6 2001 M Street N.W., Suite 600</div> <div>7 Washington, D.C. 20036</div> <div>8 (202) 682-7000</div> <div>9 priyata.patel@weil.com</div> <div>10 and</div> <div>11 KATHRYN LEICHT, ESQ.</div> <div>12 Weil, Gotshal &amp; Manges LLP</div> <div>13 767 5th Avenue</div> <div>14 New York, New York 10153</div> <div>15 (212) 310-8578</div> <div>16 kathryn.leicht@weil.com</div> <div>17</div> <div>18</div> <div>19</div> <div>20</div> <div>21</div> <div>22</div>                                                                                                                | Page 3 | <div>1 C O N T E N T S</div> <div>2 WITNESS EXAMINATION BY COUNSEL FOR</div> <div>3 DAVID A. SCOTT PETITIONER PATENT OWNER</div> <div>4 By Ms. Patel 7</div> <div>5 By Ms. Danek 116</div> <div>6</div> <div>7 E X H I B I T S</div> <div>8 SCOTT EXHIBIT NO. PAGE</div> <div>9 1 - April 2020 article entitled An open-source</div> <div>10 drug discovery platform enables ultra-large</div> <div>11 virtual screens 56</div> <div>12</div> <div>13 PREVIOUSLY MARKED EXHIBITS</div> <div>14 1001 - United States Patent Number 11,672,803 56</div> <div>15 2012 - Declaration of David A. Scott, Ph.D.</div> <div>16 in Support of Patent Owner's Response 9</div> <div>17 2013 - Curriculum Vitae of David A. Scott,</div> <div>18 Ph.D. 15</div> <div>19 2040 - Excerpt from a book entitled Protein</div> <div>20 Kinases as Drug Targets published in 2011 106</div> <div>21 - - -</div> <div>22</div> | Page 5 |

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| <p>1 PROCEEDINGS</p> <p>2 THE VIDEOGRAPHER: We are now on the</p> <p>3 record in the matter of BeiGene USA, Incorporated and</p> <p>4 BeiGene LTD v. Pharmacyclics LLC. Today's date is</p> <p>5 September 27th, 2024. The time is 8:43 a.m. This is</p> <p>6 the video recorded deposition of David Scott being</p> <p>7 taken remotely. The witness is located in Boston,</p> <p>8 Massachusetts.</p> <p>9 I'm the videographer. My name is Dewey</p> <p>10 Nelson in association with TP.One. The court</p> <p>11 reporter is Mary Grace Castleberry also in</p> <p>12 association with TP.One.</p> <p>13 Will all attorneys please identify</p> <p>14 themselves and the parties they represent beginning</p> <p>15 with the party noticing this proceeding.</p> <p>16 MS. PATEL: Good morning. This is Priyata</p> <p>17 Patel from Weil Gotshal on behalf of BeiGene. With</p> <p>18 me today is Kathryn Leicht also from Weil Gotshal.</p> <p>19 MS. DANEK: This is Brenda Danek with</p> <p>20 Latham &amp; Watkins representing Pharmacyclics in this</p> <p>21 proceeding and the witness.</p> <p>22 THE VIDEOGRAPHER: Will the court reporter</p> | <p>Page 6</p> | <p>1 A. Yes.</p> <p>2 Q. Have you ever been deposed before?</p> <p>3 A. No.</p> <p>4 Q. Have you ever testified at trial?</p> <p>5 A. No.</p> <p>6 Q. Do you understand that you're under oath</p> <p>7 today?</p> <p>8 A. Yes.</p> <p>9 Q. Is there any reason you can't provide</p> <p>10 accurate and truthful testimony today?</p> <p>11 A. No.</p> <p>12 Q. So let's go over just some quick ground</p> <p>13 rules before we get started. The court reporter is</p> <p>14 here writing down everything you say. So it's</p> <p>15 important that you provide verbal responses to my</p> <p>16 questions rather than, for example, nodding your head</p> <p>17 yes or no.</p> <p>18 Do you understand that?</p> <p>19 A. Yes.</p> <p>20 Q. And if you don't understand a question I</p> <p>21 ask, let me know and I'll clarify. If you don't ask</p> <p>22 me to clarify, I'm going to assume that you</p> | <p>Page 8</p> |
| <p>1 please administer the oath.</p> <p>2 Whereupon,</p> <p>3 DAVID A. SCOTT,</p> <p>4 was called as a witness by counsel for Petitioner,</p> <p>5 and having been duly sworn by the Notary Public, was</p> <p>6 examined and testified as follows:</p> <p>7 THE VIDEOGRAPHER: Please proceed.</p> <p>8 EXAMINATION BY COUNSEL FOR PETITIONER</p> <p>9 BY MS. PATEL:</p> <p>10 Q. Good morning, Dr. Scott.</p> <p>11 A. Good morning.</p> <p>12 Q. Could you please state your full name for</p> <p>13 the record.</p> <p>14 A. David Andrew Scott.</p> <p>15 Q. Do you understand that you're here today</p> <p>16 for a deposition in PGR2024-00009 between BeiGene and</p> <p>17 Pharmacyclics concerning U.S. Patent Number</p> <p>18 11,672,803?</p> <p>19 A. Yes.</p> <p>20 Q. Is it correct that you've submitted an</p> <p>21 expert declaration on behalf of Pharmacyclics in this</p> <p>22 proceeding?</p>                                                                                                                                                                                                                                        | <p>Page 7</p> | <p>1 understand my question.</p> <p>2 Do you understand that?</p> <p>3 A. Yes.</p> <p>4 Q. I'll try and take breaks every hour, but</p> <p>5 if you feel like you need a break sooner, just let me</p> <p>6 know.</p> <p>7 Do you understand that?</p> <p>8 A. Yes. That's very clear.</p> <p>9 Q. So you're retained by Pharmacyclics to</p> <p>10 provide testimony in this case as it pertains to the</p> <p>11 '803 patent, right?</p> <p>12 A. Yes.</p> <p>13 Q. When did you first learn about this case?</p> <p>14 A. I think it was in April of this year.</p> <p>15 Q. When did Pharmacyclics first contact you</p> <p>16 about the case?</p> <p>17 A. Around the same time. I think it was</p> <p>18 April.</p> <p>19 MS. PATEL: All right. Can we put up</p> <p>20 Exhibit 2012?</p> <p>21 (Exhibit No. 2012 was identified for</p> <p>22 the record.)</p>                                            | <p>Page 9</p> |

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| <p>Page 10</p> <p>1 MS. DANEK: You should have a copy of<br/>2 that.<br/>3 THE WITNESS: So that's the declaration?<br/>4 MS. DANEK: Yes.<br/>5 BY MS. PATEL:<br/>6 Q. So Dr. Scott, I understand you have a hard<br/>7 copy of your declaration in front of you. We've also<br/>8 shared on the screen and given you control of the<br/>9 document, so you can choose to flip through the hard<br/>10 copy or you can choose to flip through the version up<br/>11 on your computer there.<br/>12 All right. This is the declaration you<br/>13 submitted in this proceeding, right?<br/>14 A. Yes.<br/>15 Q. Before signing your declaration, did you<br/>16 review the text to make sure that everything was<br/>17 accurate and complete?<br/>18 A. Yes.<br/>19 Q. When did you start preparing your<br/>20 declaration?<br/>21 A. During the summer of this year.<br/>22 Q. How much time did you spend preparing the</p> | <p>Page 12</p> <p>1 Q. All right. This is the list of materials<br/>2 you reviewed and considered in forming your opinions,<br/>3 right?<br/>4 A. Yes.<br/>5 Q. Did you consider any other documents in<br/>6 forming your opinions?<br/>7 A. I would have read other references, but<br/>8 they would not have changed my opinion in this case.<br/>9 Q. What other references would you have read?<br/>10 A. Other references regarding BTK inhibitors<br/>11 and kinases.<br/>12 Q. Do you remember any details beyond the<br/>13 fact that these references were regarding BTK<br/>14 inhibitors and kinases?<br/>15 A. No, not specifically.<br/>16 Q. Titles or publication dates, anything like<br/>17 that?<br/>18 A. I reviewed -- I remember reading an<br/>19 article by Pan.<br/>20 Q. Is that the Pan article that's cited by<br/>21 Dr. Eck in his declaration in this proceeding?<br/>22 A. I don't know what articles are cited by</p> |
| <p>Page 11</p> <p>1 declaration?<br/>2 A. I worked with counsel several months.<br/>3 THE REPORTER: I'm sorry, I am barely<br/>4 hearing you. Is there a way to move the microphone<br/>5 closer to you?<br/>6 MS. DANEK: If you'll please, Dr. Scott,<br/>7 just speak up.<br/>8 THE WITNESS: Yes. I'm sorry. I worked<br/>9 over a period of weeks, I think perhaps months to<br/>10 prepare the declaration.<br/>11 BY MS. PATEL:<br/>12 Q. You said over a period of weeks and<br/>13 perhaps months to prepare the declaration, is that<br/>14 right?<br/>15 A. Yes.<br/>16 Q. Did you draft the declaration yourself?<br/>17 A. I worked with the attorneys to draft it.<br/>18 Q. All right. Turn to pages 5 and 6 of the<br/>19 declaration, please.<br/>20 A. I'm looking at the hard copy.<br/>21 Q. Okay. You have it in -- you're on page 5?<br/>22 A. Yes.</p>                                                   | <p>Page 13</p> <p>1 Dr. Eck.<br/>2 MS. DANEK: Dr. Scott, I think you need to<br/>3 speak up.<br/>4 THE WITNESS: I don't know what articles<br/>5 are cited by Dr. Eck, but the Pan article, I believe,<br/>6 was cited by Dr. Showalter.<br/>7 BY MS. PATEL:<br/>8 Q. Okay. So that's the one you recall<br/>9 reviewing is the Pan article that was cited by<br/>10 Dr. Showalter, is that right?<br/>11 A. Yes.<br/>12 Q. Can you turn to the last page of your<br/>13 declaration, please.<br/>14 A. Yes.<br/>15 Q. Is that your signature --<br/>16 A. Yes.<br/>17 Q. -- on that last page?<br/>18 A. Yes.<br/>19 Q. What did you do to prepare for this<br/>20 deposition?<br/>21 A. I reviewed the declaration and the<br/>22 references contained -- cited in it.</p>                                                                                                                                                                           |

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| <p>Page 14</p> <p>1 Q. Did you review anything else? There's a<br/>2 question pending. I'm not sure if you heard it, so I<br/>3 want to make sure.<br/>4 A. Oh, the question was did I review anything<br/>5 else?<br/>6 Q. Yes, that's correct. Yes.<br/>7 A. Oh, no. No, I didn't.<br/>8 Q. Okay. Did you have any meetings?<br/>9 A. Yes.<br/>10 Q. How many meetings?<br/>11 A. Two Zoom calls with the attorney and then<br/>12 I met with them in person at their office in Boston.<br/>13 Q. How many times did you meet with them in<br/>14 person?<br/>15 A. Two days.<br/>16 Q. Okay. So two Zoom calls and two in-person<br/>17 meetings.<br/>18 A. Yes.<br/>19 Q. And who was present at these meetings?<br/>20 A. Brenda Danek and Alyssa Dolan.<br/>21 Q. How long were these meetings?<br/>22 A. I think the Zoom calls were one to two</p> | <p>Page 16</p> <p>1 organic chemistry from the University of Oxford,<br/>2 right?<br/>3 A. Yes.<br/>4 Q. And you completed your Ph.D. in the year<br/>5 2000?<br/>6 A. Yes.<br/>7 Q. Then you did postdoctoral research at the<br/>8 University of Austin -- or the University of Texas in<br/>9 Austin, is that right?<br/>10 A. Correct.<br/>11 Q. And you completed that research in 2002?<br/>12 A. Yes.<br/>13 Q. Did any of your post-doc research pertain<br/>14 to irreversible kinase inhibitors?<br/>15 A. No.<br/>16 Q. And then you worked at AstraZeneca in the<br/>17 oncology research and development group from 2002 to<br/>18 2013, correct?<br/>19 A. Correct.<br/>20 Q. All right. So why don't you turn to that<br/>21 section of your CV, the AstraZeneca R&amp;D Boston<br/>22 oncology group.</p>                                                                                         |
| <p>Page 15</p> <p>1 hours and the in-person meetings were most of two<br/>2 days.<br/>3 MS. PATEL: All right. Can we put up<br/>4 Exhibit 2013.<br/>5 (Exhibit No. 2013 was identified for<br/>6 the record.)<br/>7 MS. DANEK: Dr. Scott, that should be in<br/>8 your folder there.<br/>9 THE WITNESS: Yes.<br/>10 BY MS. PATEL:<br/>11 Q. Dr. Scott, have you spoken to anyone else<br/>12 other than the attorneys about this case?<br/>13 A. No.<br/>14 Q. All right. So do you have your CV in<br/>15 front of you? Do you have Exhibit 2013 in front of<br/>16 you?<br/>17 A. Yes, I have a hard copy.<br/>18 Q. Okay. And that's your CV, right?<br/>19 A. Yes.<br/>20 Q. Is this up to date?<br/>21 A. Yes, it is up to date.<br/>22 Q. Okay. So you obtained your Ph.D. in</p>                                                                    | <p>Page 17</p> <p>1 A. Okay.<br/>2 Q. Okay. So it states here in your CV that<br/>3 you led kinase chemistry teams to develop kinase<br/>4 inhibitors, right?<br/>5 A. Yes.<br/>6 Q. Did any of your work relate to<br/>7 irreversible kinase inhibitors?<br/>8 A. No.<br/>9 Q. Did it relate to kinase inhibitors?<br/>10 A. Yes.<br/>11 Q. And did you synthesize kinase inhibitors<br/>12 during your time at AstraZeneca?<br/>13 A. I did.<br/>14 Q. You did. What is the process for<br/>15 synthesizing a kinase inhibitor?<br/>16 A. Typically you would have a specific target<br/>17 compound in mind and then you would consider<br/>18 different synthetic routes to prepare it efficiently,<br/>19 and then you would identify the starting materials<br/>20 that you would need to conduct the synthesis.<br/>21 Q. So how long would it take to do each of<br/>22 the steps you just described?</p> |

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| <p>1 A. It would depend on the target compound.</p> <p>2 Q. Which target compounds did you synthesize</p> <p>3 while at AstraZeneca?</p> <p>4 A. I synthesized compounds of a number of</p> <p>5 different chemical series.</p> <p>6 Q. Could you name one?</p> <p>7 A. I made a series of what we call amido</p> <p>8 quinolines for our CSF-1R project.</p> <p>9 MS. DANEK: Dr. Scott, if you could focus</p> <p>10 on speaking up. I just want to make sure the court</p> <p>11 reporter -- these terms are quite --</p> <p>12 THE WITNESS: I'll repeat that. I made a</p> <p>13 series of amido quinolines for our CSF-1R project.</p> <p>14 BY MS. PATEL:</p> <p>15 Q. And could you spell the amido quinoline?</p> <p>16 A. Certainly. A-m-i-d-o, q-u-i-n-o-l-i-n-e.</p> <p>17 Q. So you said one of the steps in the</p> <p>18 synthesis process would be considering different</p> <p>19 synthetic routes for the target compound, right?</p> <p>20 A. Yes. Sometimes there are multiple ways to</p> <p>21 make a compound.</p> <p>22 Q. Okay. So how long for amido quinoline did</p>                                    | <p>Page 18</p> <p>1 make it more or less difficult to synthesize it, the</p> <p>2 compound?</p> <p>3 MS. DANEK: Objection, form.</p> <p>4 THE WITNESS: The size and the complexity</p> <p>5 of a compound would determine the level of</p> <p>6 difficulty.</p> <p>7 BY MS. PATEL:</p> <p>8 Q. Okay. So a larger size compound would be</p> <p>9 a more difficult compound to synthesize, is that</p> <p>10 right?</p> <p>11 A. In some cases, but not necessarily.</p> <p>12 Q. So how does size determine the level of</p> <p>13 difficulty in synthesis?</p> <p>14 A. In some cases, a larger molecule might</p> <p>15 require additional synthetic steps, but that's not</p> <p>16 always the case.</p> <p>17 Q. What would you consider a larger molecule?</p> <p>18 A. In what context?</p> <p>19 Q. In the context of synthesizing a compound,</p> <p>20 what size compound would you might consider to be</p> <p>21 more difficult?</p> <p>22 A. In the kinase projects I've been involved</p>                            |
| <p>1 it take to consider the different synthetic routes</p> <p>2 that you might use and to decide on one?</p> <p>3 A. I couldn't give you a general response to</p> <p>4 that. It would depend on the specific target.</p> <p>5 Q. But what was the specific target that you</p> <p>6 were synthesizing in this design project?</p> <p>7 A. One set of compounds, I remember we varied</p> <p>8 the aniline substituents of the former position of</p> <p>9 the quinoline, and that was a relatively</p> <p>10 straightforward task to do and didn't require much</p> <p>11 research.</p> <p>12 Q. When you say it was a relatively</p> <p>13 straightforward task to do, what was the task that</p> <p>14 you were doing there? Was it actually synthesizing</p> <p>15 the compound or was it -- was it identifying the</p> <p>16 synthetic route that you would use to synthesize it?</p> <p>17 A. Both.</p> <p>18 Q. You said the amount of time that it takes</p> <p>19 to synthesize a compound depends on the compound</p> <p>20 itself, right?</p> <p>21 A. Yes.</p> <p>22 Q. What characteristics of a compound would</p> | <p>Page 19</p> <p>1 in, we would typically try not to -- we would prefer</p> <p>2 not to make compounds with a molecular weight above</p> <p>3 500.</p> <p>4 Q. So in your opinion, a compound -- strike</p> <p>5 that.</p> <p>6 You also said that the complexity of a</p> <p>7 compound would determine the level of difficulty in</p> <p>8 synthesizing the compound, right?</p> <p>9 A. Yes.</p> <p>10 Q. When you say complexity of a compound,</p> <p>11 what do you mean?</p> <p>12 A. It could refer to a number of things. One</p> <p>13 aspect might be the rings of the molecule or the</p> <p>14 stereochemistry.</p> <p>15 Q. What was the last thing you said?</p> <p>16 A. Stereochemistry.</p> <p>17 Q. What about the rings of the molecule could</p> <p>18 make it more complex and therefore more difficult to</p> <p>19 synthesize?</p> <p>20 A. One example would be large macrocyclic</p> <p>21 compounds with very large rings. So typically in</p> <p>22 kinase inhibitors, we would work with small,</p> |
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| <p>1 well-understood ring systems.</p> <p>2 Q. What's an example of a small,</p> <p>3 well-understood ring system?</p> <p>4 A. The quinoline I referred to in the CSF-1R</p> <p>5 inhibitors.</p> <p>6 Q. Would you -- would you consider ibrutinib</p> <p>7 to have a small, well-understood ring system?</p> <p>8 MS. DANEK: Objection, form.</p> <p>9 THE WITNESS: It's a ring system that's</p> <p>10 been used in a number of compounds.</p> <p>11 BY MS. PATEL:</p> <p>12 Q. Would you consider ibrutinib to have a</p> <p>13 small ring system?</p> <p>14 A. Its core is a bicyclic ring system.</p> <p>15 Q. Would you consider that small?</p> <p>16 A. It's a bicyclic ring system.</p> <p>17 Q. You don't know if it's small or not?</p> <p>18 MS. DANEK: Objection, form.</p> <p>19 THE WITNESS: I would want to -- it's</p> <p>20 bigger than some ring systems. It's smaller than</p> <p>21 others.</p> <p>22 BY MS. PATEL:</p>                                                                                                                                                                     | <p>Page 22</p> <p>1 Q. A compound with many stereocenters might</p> <p>2 be harder to make than a compound with just one</p> <p>3 stereocenter, is that right?</p> <p>4 A. In some cases.</p> <p>5 Q. Why?</p> <p>6 A. It would vary depending on the specific</p> <p>7 compound.</p> <p>8 Q. Why would a compound that has many stereo</p> <p>9 centers be more difficult to make than a compound</p> <p>10 that just has a single stereocenter?</p> <p>11 MS. DANEK: Objection, form.</p> <p>12 THE WITNESS: I said it might be. It</p> <p>13 would depend on the synthetic methods involved.</p> <p>14 BY MS. PATEL:</p> <p>15 Q. So when might it be easier to synthesize a</p> <p>16 compound? What synthetic methods would be involved</p> <p>17 in that case?</p> <p>18 A. In my experience, there are several</p> <p>19 synthetic reactions that are reliable and</p> <p>20 straightforward.</p> <p>21 Q. So that didn't answer my question. What</p> <p>22 synthetic methods would be involved that would make</p>                                                                  |
| <p>1 Q. Relative to other ring systems, would you</p> <p>2 say -- would you consider it small or large?</p> <p>3 MS. DANEK: Objection, form.</p> <p>4 THE WITNESS: Which other ring systems?</p> <p>5 BY MS. PATEL:</p> <p>6 Q. You testified that when synthesizing</p> <p>7 kinase inhibitors, you work with small,</p> <p>8 well-understood ring systems, right?</p> <p>9 A. I did.</p> <p>10 Q. So I'm trying to understand what you mean</p> <p>11 when you use the term "small ring system."</p> <p>12 A. The best definition of a small ring system</p> <p>13 would be a single ring such as a phenyl.</p> <p>14 Q. You also testified that stereochemistry</p> <p>15 would impact the complexity of a compound, right, and</p> <p>16 therefore the level of difficulty in synthesizing it?</p> <p>17 A. In some cases, yes. In other cases, it</p> <p>18 can be straightforward to introduce stereochemistry.</p> <p>19 Q. In what cases would it be more difficult?</p> <p>20 A. A compound with many stereocenters might</p> <p>21 be harder to make than one with just one</p> <p>22 stereocenter.</p> | <p>Page 23</p> <p>1 it easier to synthesize a compound?</p> <p>2 A. Can you explain what you mean by synthetic</p> <p>3 method?</p> <p>4 Q. Well, you testified that it might be more</p> <p>5 difficult to synthesize a compound with multiple</p> <p>6 stereo centers, but it would depend on the synthetic</p> <p>7 methods involved. So I want to understand what you</p> <p>8 mean by the synthetic methods involved and how that</p> <p>9 would impact the difficulty in synthesizing a</p> <p>10 compound with multiple stereocenters.</p> <p>11 A. By synthetic method, I was referring to</p> <p>12 synthetic reactions.</p> <p>13 Q. Why might it be more difficult to</p> <p>14 synthesize a compound with a larger ring system?</p> <p>15 A. I would have to consider a specific</p> <p>16 compound to answer that.</p> <p>17 Q. Have you ever synthesized a BTK inhibitor?</p> <p>18 A. No.</p> <p>19 Q. Would you know how to do that?</p> <p>20 A. Are you referring to a particular BTK</p> <p>21 inhibitor in particular?</p> <p>22 Q. Would you know how to synthesize</p> |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | <p>Page 24</p> <p>Page 25</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

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| <p>1 ibrutinib?</p> <p>2 A. I would want to review the information</p> <p>3 that was available.</p> <p>4 Q. Is that a yes or a no?</p> <p>5 A. If I was able to review the synthetic</p> <p>6 procedures to prepare ibrutinib, then I would be able</p> <p>7 to prepare ibrutinib.</p> <p>8 Q. When you were at AstraZeneca in 2011,</p> <p>9 would you have been able to review the synthetic</p> <p>10 procedures to prepare ibrutinib?</p> <p>11 MS. DANEK: Objection, form.</p> <p>12 THE WITNESS: I don't know.</p> <p>13 BY MS. PATEL:</p> <p>14 Q. But you would need those synthetic</p> <p>15 procedures in order to prepare it, right?</p> <p>16 MS. DANEK: Objection, form.</p> <p>17 THE WITNESS: The procedures would be very</p> <p>18 helpful.</p> <p>19 BY MS. PATEL:</p> <p>20 Q. If you didn't have those procedures, how</p> <p>21 would you go about preparing ibrutinib?</p> <p>22 A. I would review -- I would look for and</p> | <p>Page 26</p> <p>1 on a ring system impact the complexity of the</p> <p>2 compound?</p> <p>3 A. I would -- it would depend on the nature</p> <p>4 of the compound.</p> <p>5 Q. Can you give an example of a compound</p> <p>6 where the substitutions would not affect the</p> <p>7 complexity of it?</p> <p>8 A. In the series I referred to earlier, I</p> <p>9 introduced aniline substituents where the</p> <p>10 substitutions on the ring did not affect the</p> <p>11 complexity of the compound or its synthesis.</p> <p>12 Q. Why not?</p> <p>13 A. It was the same process to make the</p> <p>14 different compounds.</p> <p>15 Q. Before you actually tried and synthesize</p> <p>16 it, however, did you know that it wouldn't affect the</p> <p>17 complexity of the compound or its synthesis?</p> <p>18 A. For that series, that process didn't</p> <p>19 affect complexity and we understood that.</p> <p>20 Q. You understood that after trying it for</p> <p>21 the first time or you understood it before trying to</p> <p>22 synthesize a compound within the series?</p> <p>Page 28</p> |
| <p>1 review related procedures.</p> <p>2 Q. So in 2011, if you wanted to prepare</p> <p>3 ibrutinib, what related procedures would be available</p> <p>4 to you?</p> <p>5 MS. DANEK: Objection, form.</p> <p>6 THE WITNESS: I don't know.</p> <p>7 BY MS. PATEL:</p> <p>8 Q. Is there anything other than the ring</p> <p>9 systems and the stereochemistry that impact the</p> <p>10 complexity of a compound and therefore the difficulty</p> <p>11 in synthesizing it?</p> <p>12 A. It would depend on the nature of the</p> <p>13 particular compound.</p> <p>14 Q. When you say nature of the particular</p> <p>15 compound, what do you mean?</p> <p>16 A. The overall structure.</p> <p>17 Q. What parts of the structure?</p> <p>18 A. All of it.</p> <p>19 Q. Okay. Do you still have your CV in front</p> <p>20 of you?</p> <p>21 A. I do.</p> <p>22 Q. Actually, Dr. Scott, do the substitutions</p>                                       | <p>Page 27</p> <p>1 A. It was a well precedented reaction and we</p> <p>2 were very confident that it would be successful.</p> <p>3 Q. You've used the word "series" a couple</p> <p>4 times today, right?</p> <p>5 A. I think so, yes.</p> <p>6 Q. How do you define series?</p> <p>7 A. The way I've used it today refers to a</p> <p>8 specific ring system. But there are other ways to</p> <p>9 define series.</p> <p>10 Q. What's the specific ring system -- could</p> <p>11 you describe it -- that you used to refer to series?</p> <p>12 A. On the CSF-1R project, I referred to the</p> <p>13 amido quinolines.</p> <p>14 Q. And can you describe the ring system for</p> <p>15 that series?</p> <p>16 A. It's a bicyclic ring system with one</p> <p>17 nitrogen atom in the ring.</p> <p>18 Q. How many members in the bicyclic ring</p> <p>19 system?</p> <p>20 A. Did you say members?</p> <p>21 Q. So were each of the rings six-membered?</p> <p>22 Five-membered?</p> <p>Page 29</p>                                                                                                        |

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| <p>Page 30</p> <p>1 A. It was two six-membered rings.</p> <p>2 Q. Were they each aromatic?</p> <p>3 A. Yes.</p> <p>4 Q. If one of the rings in the system were not</p> <p>5 aromatic, would that fall within the definition of</p> <p>6 the series?</p> <p>7 MS. DANEK: Objection, form.</p> <p>8 THE WITNESS: I wouldn't refer to that as</p> <p>9 a quinoline.</p> <p>10 BY MS. PATEL:</p> <p>11 Q. What are other ways to define series?</p> <p>12 A. As a chemist, I would rely on a common</p> <p>13 structural feature, but other scientists might use</p> <p>14 other methods.</p> <p>15 Q. So it depends on the scientist, how you</p> <p>16 would define a series?</p> <p>17 A. Yeah. I think people can look at a</p> <p>18 chemical series and refer to it in different ways.</p> <p>19 Q. Okay. So back to your CV, while you were</p> <p>20 at AstraZeneca, there's a bullet you included there</p> <p>21 that says you analyzed screening data and prioritized</p> <p>22 hit series for progression on JAK2 kinase, project</p> | <p>Page 32</p> <p>1 inhibitors did you start with?</p> <p>2 MS. DANEK: Dr. Scott, just I caution you</p> <p>3 not to reveal any confidential information for</p> <p>4 AstraZeneca depending on the questions that are</p> <p>5 asked.</p> <p>6 THE WITNESS: Of course. Can you clarify</p> <p>7 what you mean by candidate inhibitor?</p> <p>8 BY MS. PATEL:</p> <p>9 Q. The goal of this project was to identify a</p> <p>10 clinical molecule that inhibits JAK2, right?</p> <p>11 A. Yes. If you mean that the goal was to</p> <p>12 develop an inhibitor of JAK2 that would go into</p> <p>13 clinical trials, yes.</p> <p>14 Q. What was the first step in developing such</p> <p>15 an inhibitor?</p> <p>16 A. We screened -- my recollection is we</p> <p>17 screened our compound collection in a JAK2 enzyme</p> <p>18 lysine.</p> <p>19 Q. What is a compound collection?</p> <p>20 A. It's a collection of compounds that an</p> <p>21 organization uses -- it's a collection of -- it's a</p> <p>22 collection of compounds.</p> |
| <p>Page 31</p> <p>1 leading to clinical candidate AZD1480.</p> <p>2 Do you see that?</p> <p>3 A. Yes.</p> <p>4 Q. Do you remember around when you were</p> <p>5 conducting this project?</p> <p>6 A. I couldn't be confident of the year.</p> <p>7 Q. Do you remember if it was closer to when</p> <p>8 you had just started at AstraZeneca or later on</p> <p>9 during your time there?</p> <p>10 A. Maybe about the middle of my time at</p> <p>11 AstraZeneca.</p> <p>12 Q. So around 2009, 2010?</p> <p>13 A. I couldn't be sure. Possibly earlier.</p> <p>14 Q. Okay. JAK2 is another tyrosine kinase,</p> <p>15 right?</p> <p>16 A. Yes.</p> <p>17 Q. And you were involved in identifying a</p> <p>18 clinical candidate molecule that inhibits JAK2,</p> <p>19 right?</p> <p>20 A. I worked on the project during the early</p> <p>21 part of the work.</p> <p>22 Q. How many clinical -- how many candidate</p>                                                                                                                      | <p>Page 33</p> <p>1 Q. And in this case, how was the compound</p> <p>2 collection identified?</p> <p>3 A. It was the collection of compounds that</p> <p>4 AstraZeneca owned at that time.</p> <p>5 Q. In drug design, how are compounds</p> <p>6 collected for screening?</p> <p>7 MS. DANEK: Objection, form.</p> <p>8 THE WITNESS: I don't understand the</p> <p>9 question exactly.</p> <p>10 BY MS. PATEL:</p> <p>11 Q. Sure. I'll rephrase.</p> <p>12 When you're designing a drug to inhibit a</p> <p>13 specific target, how do you identify the potential</p> <p>14 compounds that you would like to screen?</p> <p>15 A. In the case of a kinase inhibitor project,</p> <p>16 a company might have a collection of compounds that</p> <p>17 have shown activity against other kinases and that</p> <p>18 would often be a very good starting point for a new</p> <p>19 project.</p> <p>20 Q. So how many compounds were in the compound</p> <p>21 collection in the JAK2 project?</p> <p>22 A. I don't remember.</p>               |

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| <p>1 Q. Do you remember if it was more or less<br/>2 than 50?<br/>3 A. It would have been thousands, a large<br/>4 number.<br/>5 Q. So there would have just been thousands,<br/>6 not hundreds of thousands, right?<br/>7 A. I believe the entire AstraZeneca<br/>8 collection might have been hundreds of thousands of<br/>9 compounds. I think we did a more focused screen on<br/>10 compounds that were likely to have confirmed the<br/>11 compounds we thought could have a chance of activity<br/>12 against JAK2 and that would have been a subset of the<br/>13 larger collection.<br/>14 Q. Did you work with a modeler at any point<br/>15 in this process?<br/>16 A. Not as part of the initial screening<br/>17 effort.<br/>18 Q. Did you work with a modeler later on?<br/>19 A. There was a modeler who worked on the JAK2<br/>20 project. I don't remember if I directly interacted<br/>21 with him.<br/>22 Q. Why was a modeler not involved in the</p>                                                                                         | <p>Page 34</p> <p>1 compounds, correct?<br/>2 A. Initially, yes.<br/>3 Q. So you said a modeler was involved later<br/>4 in the project, right?<br/>5 A. Yes.<br/>6 Q. What kind of information was a modeler<br/>7 asked to provide?<br/>8 A. I don't have specific information on that<br/>9 because I had moved on from the project.<br/>10 Q. Have you ever worked with a modeler in<br/>11 your experience in drug design?<br/>12 A. Yes.<br/>13 Q. What kind of information do you typically<br/>14 ask a modeler to provide?<br/>15 A. An example would be the predictive binding<br/>16 modes of the molecule to its target.<br/>17 Q. Any other examples?<br/>18 A. An example might be whether the<br/>19 introduction of a substituent would lead to a steric<br/>20 clash.<br/>21 Q. At what phase of drug design do you<br/>22 usually involve a modeler?</p> <p>Page 36</p>                                                                                |
| <p>1 initial screening effort?<br/>2 A. It wouldn't have made sense to do that.<br/>3 The value of modeling is, once you have identified --<br/>4 one of the values of modeling is when you have<br/>5 identified a specific compound of interest.<br/>6 Q. So how did you go from the collection of<br/>7 hundreds of thousands of compounds that AstraZeneca<br/>8 had to the more focused set of compounds that you<br/>9 screened?<br/>10 A. Can you repeat that?<br/>11 Q. How did you go from the collection of the<br/>12 hundreds of thousands of compounds that AstraZeneca<br/>13 possessed to the more focused set of compounds that<br/>14 you screened?<br/>15 A. Oh, scientists within the company would<br/>16 have considered which compounds might be suitable for<br/>17 screening in a kinase project.<br/>18 Q. And how would they do that?<br/>19 A. In one instance, they might look for<br/>20 compounds that have been prepared as part of other<br/>21 kinase inhibitor projects.<br/>22 Q. So everything you screened were existing</p> | <p>Page 35</p> <p>1 A. It can be very valuable as soon as you've<br/>2 identified an active compound. It's especially<br/>3 valuable if you have a crystal structure of your<br/>4 target.<br/>5 Q. What steps would you have taken before<br/>6 involving a modeler?<br/>7 A. In the case of JAK2, we screened the<br/>8 subset of the compound collection to identify series<br/>9 of interest.<br/>10 Q. What did that screening process involve?<br/>11 A. It involved the testing of the compound<br/>12 collection in an enzyme assay.<br/>13 Q. What did the assay test for?<br/>14 A. Inhibition of JAK2.<br/>15 Q. Okay. So for -- before you involved a<br/>16 modeler, you synthesized the compounds and you ran<br/>17 assays with them, right?<br/>18 A. No.<br/>19 Q. You didn't do that?<br/>20 A. I didn't say we synthesized the compounds.<br/>21 Q. How can you run assays without having the<br/>22 actual compounds synthesized?</p> <p>Page 37</p> |

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| <p>Page 38</p> <p>1 A. The compounds were in the company compound<br/>2 collection.</p> <p>3 Q. So they were already synthesized?</p> <p>4 A. Oh, those compounds had been synthesized.</p> <p>5 Q. Understood. And is that typically the<br/>6 point where you would involve a modeler in other drug<br/>7 design projects after the screening?</p> <p>8 A. On the kinase projects I worked on at<br/>9 AstraZeneca, we would typically engage a modeler once<br/>10 we had identified an active inhibitor.</p> <p>11 Q. So after you had run the assays to<br/>12 determine whether a compound or a series of compounds<br/>13 could inhibit the target, right?</p> <p>14 A. In my experience on those projects, that's<br/>15 what we did.</p> <p>16 Q. Okay. What about your other experiences<br/>17 on drug design projects?</p> <p>18 A. On another project at AstraZeneca, it was<br/>19 a phenotypic screening project where we hadn't<br/>20 identified the specific biological target and<br/>21 therefore we couldn't use modeling to inform our<br/>22 design.</p> | <p>Page 40</p> <p>1 remember or not.</p> <p>2 A. I can't think of an example where I've<br/>3 felt I disagreed with a modeler about their work.</p> <p>4 Q. Have you ever disagreed with them about<br/>5 the results they obtained?</p> <p>6 MS. DANEK: I'm not sure they heard you,<br/>7 Dr. Scott.</p> <p>8 THE WITNESS: No.</p> <p>9 BY MS. PATEL:</p> <p>10 Q. Do you always work with a modeler in drug<br/>11 design?</p> <p>12 A. No, I gave you an example earlier of a<br/>13 project where we weren't clear on the specific<br/>14 biological target, in which case modeling would have<br/>15 very limited value. Generally for a kinase project,<br/>16 there would be sufficient structural knowledge of the<br/>17 kinase target that modeling would be very valuable.</p> <p>18 Q. If a modeler were to tell you that a<br/>19 candidate kinase inhibitor would inhibit the target<br/>20 based on their modeling, would you take them at their<br/>21 word?</p> <p>22 MS. DANEK: Objection, form.</p> |
| <p>Page 39</p> <p>1 MS. PATEL: Okay. Why don't we take a<br/>2 break.</p> <p>3 THE VIDEOGRAPHER: We are off the record.<br/>4 The time is 9:49 a.m.</p> <p>5 (Recess.)</p> <p>6 THE VIDEOGRAPHER: We are back on the<br/>7 record. The time is 10:00 a.m.</p> <p>8 BY MS. PATEL:</p> <p>9 Q. Dr. Scott, did you speak with your counsel<br/>10 during the break that we took?</p> <p>11 A. We chatted about the weather.</p> <p>12 Q. Did you speak about your testimony at all?</p> <p>13 A. No.</p> <p>14 Q. Dr. Scott, in your experience working in<br/>15 drug design, have you ever disagreed with a modeler?</p> <p>16 A. I can't think of a specifying example<br/>17 where I've disagreed.</p> <p>18 Q. Do you think you've always agreed with the<br/>19 modeler?</p> <p>20 A. I don't know.</p> <p>21 Q. You don't remember? And that's okay if<br/>22 you don't remember. I just want to understand if you</p>                                                                                                                                                      | <p>Page 41</p> <p>1 THE WITNESS: I would want to understand<br/>2 the work they had done and the information the model<br/>3 was based upon.</p> <p>4 BY MS. PATEL:</p> <p>5 Q. Would you do any additional testing to<br/>6 confirm that they were correct?</p> <p>7 A. I'm not sure I understand what you mean by<br/>8 testing.</p> <p>9 Q. Would you run an assay to confirm that the<br/>10 inhibitor actually inhibits the target?</p> <p>11 A. Oh, I see. Yes, it's valuable to validate<br/>12 predictions of modeling with data, and that's<br/>13 something that we would have done.</p> <p>14 Q. Okay.</p> <p>15 MS. PATEL: Let's -- can we put up tab 3,<br/>16 please, and drop it into the link? Or drop the link<br/>17 into the messaging?</p> <p>18 BY MS. PATEL:</p> <p>19 Q. Okay. Dr. Scott, are you able to control<br/>20 the PDF that's up on your screen there?</p> <p>21 A. Yes. It's a little awkward, but it's<br/>22 possible.</p>                                                          |

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| <p>1 Q. So why don't you turn to the first page.</p> <p>2 A. Okay.</p> <p>3 Q. Do you see this is an article titled An</p> <p>4 open-source drug discovery platform enables</p> <p>5 ultra-large virtual screens?</p> <p>6 A. Yes.</p> <p>7 Q. Do you recognize this article?</p> <p>8 A. I do.</p> <p>9 Q. You're one of the coauthors, right?</p> <p>10 A. Yes.</p> <p>11 Q. And this article was published in April of</p> <p>12 2020, correct?</p> <p>13 A. Yes.</p> <p>14 Q. And the article relates to virtual</p> <p>15 screening, right?</p> <p>16 A. Yes.</p> <p>17 Q. What is virtual screening?</p> <p>18 A. It's the in silico screening of compounds.</p> <p>19 Q. Can you turn to page 2.</p> <p>20 A. Okay.</p> <p>21 Q. Do you see that first paragraph on top?</p> <p>22 A. Yes.</p>                                                                                                                                                                                                                                                       | <p>Page 42</p> <p>1 drugs today, right, and that's in part due to</p> <p>2 time-consuming wet-lab experiments.</p> <p>3 MS. DANEK: Objection, form.</p> <p>4 THE WITNESS: A significant part of the</p> <p>5 drug development is taken up by the clinical trials</p> <p>6 stage of a project.</p> <p>7 BY MS. PATEL:</p> <p>8 Q. So when it says time-consuming wet-lab</p> <p>9 experiments, that's referring to clinical trials?</p> <p>10 A. I don't think so. But a large part of</p> <p>11 development time of the 10-year -- average 10 years</p> <p>12 would be clinical development.</p> <p>13 Q. But it's -- part of the 10 years is also</p> <p>14 due to these wet-lab experiments, right?</p> <p>15 A. Of course.</p> <p>16 Q. What are some examples of these wet-lab</p> <p>17 experiments?</p> <p>18 A. Compound testing would be an example.</p> <p>19 Q. What specific tests?</p> <p>20 A. Testing in an enzyme assay would be an</p> <p>21 example.</p> <p>22 Q. Any others?</p> <p>Page 44</p>                                    |
| <p>1 Q. Do you see where it says that SBVS or</p> <p>2 structure-based virtual screening -- or actually,</p> <p>3 sorry, do you see where it says, "On average, an</p> <p>4 approved drug today costs 2 to 3 billion and takes</p> <p>5 over 10 years to develop. In part, this is due to</p> <p>6 expensive and time-consuming wet-lab experiments,</p> <p>7 poor initial hit compounds, and the high attrition</p> <p>8 rates in the preclinical phases"?</p> <p>9 A. Yes.</p> <p>10 Q. What does time-consuming wet-lab</p> <p>11 experiments refer to?</p> <p>12 A. That would refer to experiments in a</p> <p>13 research lab rather than on a computer.</p> <p>14 Q. And you consider them time-consuming,</p> <p>15 right?</p> <p>16 MS. DANEK: Objection, form.</p> <p>17 THE WITNESS: Some experiments take longer</p> <p>18 than others. It depends on the nature of the</p> <p>19 experiment.</p> <p>20 BY MS. PATEL:</p> <p>21 Q. That's all you said here, though, right?</p> <p>22 You referred to how it takes over 10 years to develop</p> | <p>Page 43</p> <p>1 A. Testing a compound's solubility would be</p> <p>2 another example.</p> <p>3 Q. Anything else?</p> <p>4 A. The synthesis of a compound would be a</p> <p>5 wet-lab experiment.</p> <p>6 Q. What are poor initial hit compounds?</p> <p>7 A. I didn't draft this paper myself. I had a</p> <p>8 very minor role in this project. My assumption is</p> <p>9 the scientist that wrote this was referring to a</p> <p>10 compound that was challenging to optimize.</p> <p>11 Q. You're a coauthor on this paper, right?</p> <p>12 A. I am a coauthor. As I said, I had a very</p> <p>13 minor role in this -- in this project.</p> <p>14 Q. Did you read this paper before it was</p> <p>15 submitted to the journal for publication?</p> <p>16 A. I did.</p> <p>17 Q. Okay. So did you agree with what was</p> <p>18 written in here?</p> <p>19 A. I might have phrased some of the</p> <p>20 discussion differently.</p> <p>21 Q. Do you commonly sign your name to papers</p> <p>22 that you disagree with?</p> <p>Page 45</p> |

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| <p>1 MS. DANEK: Objection action form.</p> <p>2 THE WITNESS: I didn't say I disagreed</p> <p>3 with this, but I said I might have phrased some of</p> <p>4 the language differently.</p> <p>5 BY MS. PATEL:</p> <p>6 Q. Okay. But you agree with the substance of</p> <p>7 it, right?</p> <p>8 A. I don't remember reading anything in here</p> <p>9 that I strongly disagreed with.</p> <p>10 Q. Okay. And then where it says high</p> <p>11 attrition rates in the preclinical phases, what is</p> <p>12 that referring to?</p> <p>13 A. Again, I didn't write this myself. And</p> <p>14 that phrase could mean different things. It may</p> <p>15 refer to projects not progressing into the clinic,</p> <p>16 but I'm not certain.</p> <p>17 Q. Okay. Do you see the next sentence there</p> <p>18 that says that "Structure-based virtual screening or</p> <p>19 SBVS has the potential to mitigate these problems"?</p> <p>20 Do you see that?</p> <p>21 A. Yes.</p> <p>22 Q. Do you see then where it says that "The</p>       | <p>Page 46</p> <p>1 A. Yes.</p> <p>2 Q. "A highly automated and versatile</p> <p>3 open-source platform with perfect scaling behavior</p> <p>4 that is able to prepare and efficiently screen</p> <p>5 ultra-large ligand libraries of compounds."</p> <p>6 So I guess I could ask the same question</p> <p>7 to you is what does it mean to be able to prepare</p> <p>8 ultra-large ligand libraries of compounds?</p> <p>9 A. My understanding is that it's referring to</p> <p>10 the assembly of a list of virtual compound</p> <p>11 structures.</p> <p>12 Q. And as you said, this capability was not</p> <p>13 available prior to VirtualFlow, right?</p> <p>14 MS. DANEK: Objection, form.</p> <p>15 THE WITNESS: I haven't fully reviewed</p> <p>16 this field. It's not an area of my expertise. But</p> <p>17 my understanding is that this paper describes an</p> <p>18 advance in the field of virtual screening.</p> <p>19 BY MS. PATEL:</p> <p>20 Q. Do you see the second paragraph on that</p> <p>21 same page?</p> <p>22 A. I'm sorry, I moved the page on the screen.</p> <p>Page 48</p> |
| <p>1 ability, however, to carry out large-scale SBVSs on</p> <p>2 computer clusters in an accessible, efficient, and</p> <p>3 flexible manner has remained elusive"?</p> <p>4 Do you see that?</p> <p>5 A. Yes.</p> <p>6 Q. What does it mean to carry out large-scale</p> <p>7 SBVSs on computer clusters?</p> <p>8 A. My understanding is this paper is</p> <p>9 describing a process to scale -- to test -- virtually</p> <p>10 screen very large numbers of compounds in a way that</p> <p>11 had not been routine previously.</p> <p>12 Q. And so this new platform as of the</p> <p>13 publishing of this article is called VirtualFlow,</p> <p>14 right?</p> <p>15 A. Yes.</p> <p>16 Q. And that is able to prepare and</p> <p>17 efficiently screen ultra-large ligand libraries of</p> <p>18 compounds, right?</p> <p>19 A. Can you clarify what you mean by prepare?</p> <p>20 Q. So do you see -- well -- do you see where</p> <p>21 it says, "Here we designed VirtualFlow"?</p> <p>22 Do you see that?</p> <p>Page 47</p> | <p>1 I'm looking at a hard copy. Can you give me a page</p> <p>2 number?</p> <p>3 Q. Page 2.</p> <p>4 A. So second paragraph starting with --</p> <p>5 Q. It states, "Repeated optimization of lead</p> <p>6 compounds." Do you see that?</p> <p>7 A. Okay. Yes.</p> <p>8 Q. Do you see where it says, "Repeated</p> <p>9 optimization of lead compounds and late-stage failure</p> <p>10 of drug candidates are the primary causes of longer</p> <p>11 development times and increased costs in drug</p> <p>12 development"?</p> <p>13 A. Yes, I see that.</p> <p>14 Q. So this says that repeated optimization of</p> <p>15 lead compounds increases the time and costs of drug</p> <p>16 development, right?</p> <p>17 A. I'm sorry, did you just repeat that first</p> <p>18 sentence? Sorry. Can you repeat that?</p> <p>19 Q. That's fine. Sure. We can strike that.</p> <p>20 Why is repeated optimization necessary?</p> <p>21 A. In some cases, a lead compound might not</p> <p>22 meet all the objectives of a drug discovery project.</p> <p>Page 49</p>                                        |

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| <p>Page 50</p> <p>1 Q. So is this referring to additional<br/>2 validation that would need to occur?</p> <p>3 A. I don't know.</p> <p>4 Q. About halfway down that same paragraph, do<br/>5 you see where it says, "The scale of a virtual screen<br/>6 is of central importance because the more compounds<br/>7 that are screened, (a) the lower the rate of false<br/>8 positives, and (b) the more favorable the quality of<br/>9 the lead compounds (e.g., higher-affinity binders)."</p> <p>10 Do you see that?</p> <p>11 A. Yes.</p> <p>12 Q. So a virtual screen involves modeling or<br/>13 docking compounds, right?</p> <p>14 A. Yes.</p> <p>15 Q. And what this is saying is that the more<br/>16 compounds that are modeled or docked, the lower the<br/>17 rates of false positives, right?</p> <p>18 A. That's what it says.</p> <p>19 Q. Why is that?</p> <p>20 A. Again, I'm not an expert in virtual<br/>21 screening. I was happy to accept that my author's<br/>22 conclusions were valid in this paper.</p>                                        | <p>Page 52</p> <p>1 something that we did at AstraZeneca, and we had a<br/>2 number of kinase projects at that time.</p> <p>3 Q. What's the distinction between virtual<br/>4 screening and modeling?</p> <p>5 A. Modeling -- one distinction is that<br/>6 modeling would typically involve a small number of<br/>7 specific compounds where their method of binding was<br/>8 understood to some extent, to some extent. Virtual<br/>9 screening involves huge numbers of -- can involve<br/>10 huge numbers of compounds and its goal is to identify<br/>11 some compounds that might bind.</p> <p>12 Q. Okay. Could you turn back to your<br/>13 declaration, please.</p> <p>14 A. Okay. I have the hard copy.</p> <p>15 Q. Okay. Wonderful. Can you turn to<br/>16 paragraph 12.</p> <p>17 A. Okay.</p> <p>18 Q. So in paragraph 12, you provide your<br/>19 proposed definition of a POSA, right?</p> <p>20 A. Yes.</p> <p>21 Q. And you understand when I say POSA, I mean<br/>22 person of ordinary skill in the art, right?</p> |
| <p>Page 51</p> <p>1 Q. So in 2011, there were fewer known BTKIs<br/>2 than there are today, right?</p> <p>3 A. Yes.</p> <p>4 Q. So there would have been a higher rate of<br/>5 false positives from virtual screening in 2011 than<br/>6 today, right?</p> <p>7 MS. DANEK: Objection, form.</p> <p>8 THE WITNESS: If you're talking about<br/>9 virtual screening generally, I couldn't say. Virtual<br/>10 screen -- my understanding is virtual screening has<br/>11 most value for challenging drug discovery targets<br/>12 where the structural information is not well<br/>13 understood and where there's limited precedence of<br/>14 existing drugs or clinical compounds.</p> <p>15 I'm not aware of virtual screening efforts<br/>16 for kinases because kinases are typically well<br/>17 understood in terms of their structure and compound<br/>18 binding.</p> <p>19 BY MS. PATEL:</p> <p>20 Q. So do you think in 2011, a POSA would not<br/>21 have pursued virtual screening for kinases?</p> <p>22 A. I'm not aware of any examples. It was not</p> | <p>Page 53</p> <p>1 A. Yes.</p> <p>2 Q. Can you go to paragraph 14.</p> <p>3 A. Yes.</p> <p>4 Q. So there you state that you would have<br/>5 qualified as a member of the POSA team as of the<br/>6 claimed June 3rd, 2011 priority date of the '803<br/>7 patent, right?</p> <p>8 A. Yes.</p> <p>9 Q. So turning back to paragraph 12, your<br/>10 definition of a POSA, you state that a POSA would<br/>11 have been a team, right?</p> <p>12 A. Yes.</p> <p>13 Q. And one member of that team would have at<br/>14 least a medical degree with training in hematology<br/>15 and oncology, including several years of clinical<br/>16 experience in treating hematologic malignancies,<br/>17 right?</p> <p>18 A. Yes.</p> <p>19 Q. You don't contend that you would have been<br/>20 this member of the team, right?</p> <p>21 A. I don't have any clinical training.</p> <p>22 Q. And then you say in that same paragraph</p>                                                                                                      |

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| <p>1 that another member or members would have at least a<br/>2 Ph.D. in chemistry, organic chemistry, or related<br/>3 field with training as a medicinal chemist and in the<br/>4 structure of kinases or structure-activity<br/>5 relationships of kinase inhibitors, right?<br/>6 A. Yes.<br/>7 Q. You contend that you would have been one<br/>8 of these members, right?<br/>9 A. Yes.<br/>10 Q. Do you have training as a medicinal<br/>11 chemist in the structure of kinases?<br/>12 A. I have training as a medicinal chemist.<br/>13 Q. And you don't have training in the<br/>14 structure of kinases?<br/>15 A. I'm not a structural biologist.<br/>16 Q. So no?<br/>17 A. It depends what you mean by "training in<br/>18 the structure."<br/>19 Q. What did you mean, because this is your<br/>20 definition?<br/>21 A. Oh.<br/>22 Q. Do you see it says, "With training as a</p>                                                                                                                 | Page 54 | <p>1 Q. What are some other examples of roles or<br/>2 jobs that a person could have that would allow them<br/>3 to have training in the structure-activity<br/>4 relationships of kinase inhibitors?<br/>5 A. Somebody involved in modeling.<br/>6 Q. Okay. You can put that aside for a<br/>7 second.<br/>8 MS. PATEL: Can we put up Exhibit 1001,<br/>9 the '803 patent, please.<br/>10 (Exhibit No. 1001 was identified for<br/>11 the record.)<br/>12 MS. PATEL: While we're doing that, let's<br/>13 go ahead and mark tab 3 as Scott Exhibit 1.<br/>14 (Scott Exhibit No. 1 was marked for<br/>15 identification.)<br/>16 MS. DANEK: Is that the previous exhibit<br/>17 that you introduced? Okay.<br/>18 MS. PATEL: Yeah.<br/>19 BY MS. PATEL:<br/>20 Q. All right. Dr. Scott, do you have the<br/>21 '803 patent in front of you?<br/>22 A. I do.</p> | Page 56 |
| <p>1 medicinal chemist and in the structure of kinases"?<br/>2 So what did you mean when you said with training in<br/>3 the structure of kinases?<br/>4 A. It could mean an awareness of the<br/>5 structure of kinases, their two-dimensional<br/>6 structure.<br/>7 Q. And do you have training in the structure<br/>8 of kinases?<br/>9 A. I'm aware of the structure of kinases. I<br/>10 have training in structure-activity relationships,<br/>11 which is also part of my definition.<br/>12 Q. And what does training in the<br/>13 structure-activity relationship of kinase inhibitors<br/>14 entail?<br/>15 A. It entails in experience in how do the<br/>16 structure of compounds interact with the kinase.<br/>17 Q. How would a person obtain such training?<br/>18 A. In my case, I obtained that through<br/>19 working as a medicinal chemist on a kinase project.<br/>20 Q. So a single kinase project is sufficient<br/>21 training in your view, is that right?<br/>22 A. It could be.</p> | Page 55 | <p>1 Q. You have Exhibit 1001 in front of you,<br/>2 right?<br/>3 A. Yes.<br/>4 Q. And that's the '803 patent?<br/>5 A. Yes.<br/>6 Q. You understand that this is the patent<br/>7 that's at issue in this case?<br/>8 A. Yes.<br/>9 Q. Have you reviewed the patent?<br/>10 A. I'm familiar with it.<br/>11 Q. Have you reviewed it?<br/>12 A. It depends on your exact definition of<br/>13 reviewed, but I have -- I'm familiar with it. I've<br/>14 looked at it.<br/>15 Q. Have you read through it?<br/>16 A. I haven't read every word, but I've read<br/>17 sections of it that I felt were relevant.<br/>18 Q. Which sections of it did you review?<br/>19 A. I reviewed the claims.<br/>20 Q. Any other sections?<br/>21 A. I don't remember.<br/>22 Q. Okay. Can you turn to column 45.</p>                                                          | Page 57 |

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| <p>Page 58</p> <p>1 A. Okay.</p> <p>2 Q. Okay. Thanks. Look down to line 56.</p> <p>3 A. Okay.</p> <p>4 Q. Do you see where it says, "The BTK</p> <p>5 inhibitor compounds described herein are selective</p> <p>6 for BTK and kinases having a cysteine residue in an</p> <p>7 amino acid sequence position of the tyrosine kinase</p> <p>8 that is homologous to the amino acid sequence</p> <p>9 position of cysteine 481 in BTK"?</p> <p>10 A. Yes.</p> <p>11 Q. That's describing how the claimed</p> <p>12 compounds covalently bind cysteine 481 of BTK, right?</p> <p>13 A. Yes.</p> <p>14 Q. And then it goes on to say that</p> <p>15 "Generally, an irreversible inhibitor compounds of</p> <p>16 BTK used in the methods described herein is</p> <p>17 identified or characterized in an in vitro assay."</p> <p>18 And then after that sentence, it says,</p> <p>19 "Such assays are useful to determine an in vitro IC50</p> <p>20 for an irreversible BTK inhibitor compound."</p> <p>21 Do you see that?</p> <p>22 A. I do.</p>                    | <p>Page 60</p> <p>1 MS. DANEK: Objection, form.</p> <p>2 THE WITNESS: The IC50 value provides</p> <p>3 information on compound activity.</p> <p>4 BY MS. PATEL:</p> <p>5 Q. Would a POSA have considered a BTKi with</p> <p>6 an IC50 value of greater than 10,000 nanomolar as</p> <p>7 active?</p> <p>8 A. I don't know.</p> <p>9 Q. Why not?</p> <p>10 A. If it's greater than 10,000, then it's not</p> <p>11 defined.</p> <p>12 Q. I don't understand what you mean by "then</p> <p>13 it's not defined."</p> <p>14 A. It's not a specific value.</p> <p>15 Q. Okay. Would a POSA have considered a BTKi</p> <p>16 with an IC50 value of 10,000 nanomolar as active?</p> <p>17 A. That could be termed as active compound.</p> <p>18 Q. I don't think we caught that. You said</p> <p>19 that could be --</p> <p>20 A. That could be termed as an active</p> <p>21 compound.</p> <p>22 Q. Could you explain your reasoning?</p>                                                                                          |
| <p>Page 59</p> <p>1 Q. So these statements are describing assays</p> <p>2 that are used to identify binding of BTK inhibitor to</p> <p>3 BTK, right?</p> <p>4 A. That's my understanding.</p> <p>5 Q. And it specifically mentions assays to</p> <p>6 determine the IC50 value of an irreversible BTK,</p> <p>7 right?</p> <p>8 A. It does.</p> <p>9 Q. What does an IC50 value tell you?</p> <p>10 A. It provides information on the compound</p> <p>11 concentration required for an effect on a target.</p> <p>12 Q. So in this context, it tells you how much</p> <p>13 of a BTKi is needed to inhibit BTK activity by half,</p> <p>14 right?</p> <p>15 A. Can you repeat that?</p> <p>16 Q. In the context of the '803 patent, an IC50</p> <p>17 value tells you how much of a particular BTKi is</p> <p>18 needed to inhibit BTK activity by half, right?</p> <p>19 A. Yes. That's essentially correct, yes.</p> <p>20 Q. So the IC50 value can tell a POSA whether</p> <p>21 a BTKi candidate is active or inactive in inhibiting</p> <p>22 BTK, right?</p> | <p>Page 61</p> <p>1 A. If it has activity of -- remind me what</p> <p>2 number you gave.</p> <p>3 Q. 10,000 nanomolar.</p> <p>4 A. If it has -- if the IC50 is 10,000</p> <p>5 nanomolar, then that's its activity level. It has</p> <p>6 activity.</p> <p>7 Q. What IC50 value would you consider to be</p> <p>8 indicative of an inactive molecule?</p> <p>9 A. If the assay is unable to record a level</p> <p>10 of activity, then the compound would be inactive in</p> <p>11 that assay.</p> <p>12 Q. So in that instance, what would be the</p> <p>13 IC50 value?</p> <p>14 A. There wouldn't be an IC50 value.</p> <p>15 Q. When you were working at AstraZeneca, if a</p> <p>16 candidate inhibitor had an IC50 value of 10,000</p> <p>17 nanomolar, would you consider that compound to be</p> <p>18 active?</p> <p>19 A. Can you remind me what you mean by</p> <p>20 "candidate inhibitor"?</p> <p>21 Q. An inhibitor for which you're unsure -- or</p> <p>22 strike that. A compound for which you're unsure</p> |

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| <p>1 whether or not it inhibits a target.</p> <p>2 A. If we tested a compound and the IC50 was</p> <p>3 10,000 nanomolar, that would be an active compound.</p> <p>4 Q. And would you pursue that compound in drug</p> <p>5 design?</p> <p>6 MS. DANEK: Objection, form.</p> <p>7 THE WITNESS: It would depend on the</p> <p>8 project.</p> <p>9 BY MS. PATEL:</p> <p>10 Q. In your experience in drug design, have</p> <p>11 you ever advanced a compound that has an IC50 value</p> <p>12 as high as 10,000 nanomolar?</p> <p>13 A. What do you mean by "advanced"?</p> <p>14 Q. Recommended pursuing as a clinical</p> <p>15 compound.</p> <p>16 A. And what do you mean by pursuing as a</p> <p>17 clinical compound?</p> <p>18 Q. What is the goal of drug design?</p> <p>19 A. To develop new therapeutic agents.</p> <p>20 Q. Okay. In your experience working in drug</p> <p>21 design, have you ever identified a compound that has</p> <p>22 an IC50 value as high as 10,000 nanomolar and</p>                                                        | <p>Page 62</p> <p>1 IC50 value of less than 2,000 nanomolar?</p> <p>2 A. I believe so.</p> <p>3 Q. What about less than 1,000 nanomolar?</p> <p>4 A. Yes, I believe so.</p> <p>5 Q. Would you ever recommend pursuing as a new</p> <p>6 therapeutic agent a kinase inhibitor that has greater</p> <p>7 than 1,000 nanomolar of IC50 value?</p> <p>8 A. I don't know.</p> <p>9 Q. What more would you need to know?</p> <p>10 A. It might depend on the particular kinase.</p> <p>11 Q. Would you ever recommend pursuing as a new</p> <p>12 therapeutic agent a BTK inhibitor that has an IC50</p> <p>13 value of greater than a thousand nanomolar?</p> <p>14 A. I don't know.</p> <p>15 Q. Why not?</p> <p>16 A. I haven't worked directly on BTK. I don't</p> <p>17 have all the information I might need to make that</p> <p>18 decision.</p> <p>19 Q. So you think that it all depends on the</p> <p>20 particular kinase that you're working with, but</p> <p>21 because you haven't worked with BTK before, you can't</p> <p>22 answer that question, right?</p> <p>Page 64</p> |
| <p>1 recommended that it could be a potential new</p> <p>2 therapeutic agent?</p> <p>3 A. No. In my experience in kinase projects,</p> <p>4 we've looked for compounds with better activity.</p> <p>5 Q. Is there a particular cutoff you would</p> <p>6 have used for IC50 value in kinase projects?</p> <p>7 A. No hard cutoff, no.</p> <p>8 Q. But 10,000 nanomolars is too high, right?</p> <p>9 A. We would typically prioritize compounds</p> <p>10 that had lower activity.</p> <p>11 Q. Lower than 10,000?</p> <p>12 A. Yes.</p> <p>13 Q. What about lower than 5,000?</p> <p>14 A. Typically we would prioritize the most --</p> <p>15 some of -- the most active compounds we have.</p> <p>16 Q. And would the most active compounds ever</p> <p>17 be as high as 5,000 nanomolar?</p> <p>18 A. On the kinase projects I've worked on, we</p> <p>19 had more active compounds than that.</p> <p>20 Q. Did you have -- were these more active</p> <p>21 compounds -- strike that.</p> <p>22 Did these more active compounds have an</p> <p>Page 63</p> | <p>1 MS. DANEK: Objection, form.</p> <p>2 THE WITNESS: The IC50 value of a compound</p> <p>3 necessarily would likely be different between</p> <p>4 different kinases.</p> <p>5 BY MS. PATEL:</p> <p>6 Q. Right. So you can't provide any opinions</p> <p>7 on what a POSA would consider to be an active or</p> <p>8 inactive IC50 value for a BTK inhibitor because it</p> <p>9 would depend on any differences between different</p> <p>10 kinases and you don't have experience with BTK,</p> <p>11 right?</p> <p>12 MS. DANEK: Objection, form.</p> <p>13 THE WITNESS: Could you repeat that again?</p> <p>14 BY MS. PATEL:</p> <p>15 Q. You can't provide opinions on IC50 values</p> <p>16 in the context of a BTK inhibitor because you don't</p> <p>17 have experience with BTK, right?</p> <p>18 MS. DANEK: Objection, form.</p> <p>19 THE WITNESS: I haven't directly worked on</p> <p>20 a BTK inhibitor project.</p> <p>21 BY MS. PATEL:</p> <p>22 Q. And because of that, you don't think you</p> <p>Page 65</p>                                                         |

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| <p>1 can provide opinions on IC50 values in the context of</p> <p>2 BTK inhibitors, right?</p> <p>3 MS. DANEK: Objection, form.</p> <p>4 THE WITNESS: I don't have a full</p> <p>5 understanding of what would be needed for a BTK</p> <p>6 inhibitor.</p> <p>7 BY MS. PATEL:</p> <p>8 Q. So the answer is yes, right?</p> <p>9 A. I haven't fully considered what it would</p> <p>10 take to identify a good BTK inhibitor.</p> <p>11 Q. Okay.</p> <p>12 MS. PATEL: Why don't we take a break.</p> <p>13 THE VIDEOGRAPHER: We are off the record.</p> <p>14 The time is 10:57 a.m.</p> <p>15 (Recess.)</p> <p>16 THE VIDEOGRAPHER: We are back on the</p> <p>17 record. The time is 11:05 a.m.</p> <p>18 BY MS. PATEL:</p> <p>19 Q. Dr. Scott, can you turn to paragraph 33 of</p> <p>20 your declaration, please.</p> <p>21 MS. DANEK: That's three-three?</p> <p>22 MS. PATEL: Correct.</p>                                                                               | <p>Page 66</p> | <p>1 Q. So a POSA wouldn't use a compound with a</p> <p>2 molecular weight of 510, is that right?</p> <p>3 MS. DANEK: Objection, form.</p> <p>4 THE WITNESS: No.</p> <p>5 BY MS. PATEL:</p> <p>6 Q. But if it violates Lipinski's rules, why</p> <p>7 would a POSA use a compound that has a molecular</p> <p>8 weight of 510 in 2011?</p> <p>9 A. I said these were guidelines rather than</p> <p>10 hard rules.</p> <p>11 Q. Okay. So would a POSA in 2011 pursue it</p> <p>12 as a potential drug candidate if it otherwise seemed</p> <p>13 promising?</p> <p>14 A. They might.</p> <p>15 Q. The fact that it's greater than 500</p> <p>16 wouldn't on its own disqualify it from being pursued</p> <p>17 as a potential therapeutic to a POSA, right?</p> <p>18 A. A chemist would look at all the properties</p> <p>19 of a compound and all the data to decide which ones</p> <p>20 to pursue.</p> <p>21 Q. And would that also be true if it had a</p> <p>22 molecular weight of 550?</p>                                                                                                                                 | <p>Page 68</p> |
| <p>1 THE WITNESS: Yes, I'm there.</p> <p>2 BY MS. PATEL:</p> <p>3 Q. In this paragraph, you discuss Lipinski's</p> <p>4 rule of 5, correct?</p> <p>5 A. Yes.</p> <p>6 Q. And you state that Lipinski's rules were</p> <p>7 compound designed guidelines in 2011, right?</p> <p>8 A. That's correct.</p> <p>9 Q. Do you think that these were rigid rules</p> <p>10 or more flexible guidelines?</p> <p>11 A. These were helpful guidelines.</p> <p>12 Q. And one of these guidelines identified</p> <p>13 that compounds are likely to show poor absorption</p> <p>14 where their molecular rate is greater than 500</p> <p>15 Dalton, right?</p> <p>16 A. That's one of the parameters in the rules,</p> <p>17 yes.</p> <p>18 Q. In 2011, would a POSA expect that a</p> <p>19 compound with a molecular weight of 510 would violate</p> <p>20 Lipinski's rules?</p> <p>21 A. The rules of a cutoff of 500 for molecular</p> <p>22 weight. 510 is above that obviously.</p> | <p>Page 67</p> | <p>1 A. The value in Lipinski rules is to steer</p> <p>2 chemists to areas with the highest probability of</p> <p>3 success. So the farther from those guidelines,</p> <p>4 probability of success would be less.</p> <p>5 Q. But you wouldn't know for sure that a</p> <p>6 compound that has a molecular weight of 550, for</p> <p>7 example, would not work simply because it violates</p> <p>8 Lipinski's rules, right?</p> <p>9 A. And what do you mean by "work"?</p> <p>10 Q. Have sufficient absorption.</p> <p>11 A. Oh. No, there's no direct correlation</p> <p>12 between molecular weight and absorption.</p> <p>13 Q. So why then is one of Lipinski's rules</p> <p>14 that compounds greater than 500 are -- I suppose,</p> <p>15 what do you view as one of his rules with regard to</p> <p>16 molecular weight?</p> <p>17 A. Well, the rule states that above 500, the</p> <p>18 chances of a compound having good absorption</p> <p>19 decrease.</p> <p>20 Q. But there's no direct correlation between</p> <p>21 molecular weight and absorption, right?</p> <p>22 A. There's no linear correlation in the</p> | <p>Page 69</p> |

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| <p>1 strict sense. There's a range of molecular weights</p> <p>2 that have a better chance of absorption than others.</p> <p>3 And Lipinski proposed 500, so --</p> <p>4 Q. In your experience reviewing drug design,</p> <p>5 have you ever advanced a clinical candidate that has</p> <p>6 a molecular weight of greater than 500?</p> <p>7 A. Yes.</p> <p>8 Q. What was that drug?</p> <p>9 A. It's a drug on a project I'm currently</p> <p>10 working on.</p> <p>11 Q. Okay. And are you able to disclose the</p> <p>12 name? Or that's all right if you can't. I just want</p> <p>13 to --</p> <p>14 A. I prefer not to discuss details.</p> <p>15 Q. That's fine. What is the molecular weight</p> <p>16 of that particular candidate that you advanced?</p> <p>17 A. I cannot disclose that.</p> <p>18 Q. All right. But it's greater than 500?</p> <p>19 A. Yes.</p> <p>20 Q. Let's turn back to the '803 patent,</p> <p>21 Exhibit 1001. Are you there?</p> <p>22 A. Yes.</p>                                                                                                     | Page 70 | <p>1 a compound with a total molecular weight of over 500?</p> <p>2 A. Partly, yes, that's one of the reasons.</p> <p>3 Q. Could you turn to column 9 of the patent.</p> <p>4 A. Okay.</p> <p>5 Q. Have you reviewed -- actually, I'm sorry,</p> <p>6 column 19.</p> <p>7 A. Okay. I'm there.</p> <p>8 Q. Have you reviewed this column 19 before?</p> <p>9 A. Not carefully, no.</p> <p>10 Q. But you have looked at it before?</p> <p>11 A. I was aware there was a list of</p> <p>12 substituents.</p> <p>13 Q. Okay. So let's go down to that list. It</p> <p>14 starts at line 57. Do you see that?</p> <p>15 A. Oh, yes. The text, yes.</p> <p>16 Q. Do you see where it says, "The term</p> <p>17 'optionally substituted' or 'substituted' means"?</p> <p>18 Do you see that?</p> <p>19 A. Yes.</p> <p>20 Q. Have you reviewed that paragraph before?</p> <p>21 A. I don't recall, but I'm looking at it now.</p> <p>22 Q. Okay. So do you see that first sentence</p>                                                                                 | Page 72 |
| <p>1 Q. Can you turn closer to the back of the</p> <p>2 patent where it has the claims listed. Let's start</p> <p>3 with claim 1. Let me though when you get there.</p> <p>4 A. That's paragraph 151 -- or column 151.</p> <p>5 Q. Yes, I think that's right. So are you</p> <p>6 looking at claim 1?</p> <p>7 A. Yes.</p> <p>8 Q. Do you see where it says -- right under</p> <p>9 the picture of the Z prime structure -- do you see</p> <p>10 where it says, "Z prime is an optionally substituted</p> <p>11 fused heterocyclic ring system"?</p> <p>12 A. Yes.</p> <p>13 Q. Do you agree that the claim language</p> <p>14 allows for optional substitutions on Z prime?</p> <p>15 A. Yes.</p> <p>16 Q. And it's your opinion that the optional</p> <p>17 substitutions on Z prime should not be bulky or have</p> <p>18 a high molecular weight, right?</p> <p>19 A. I think too many large or bulky</p> <p>20 substituents would reduce the chances of success.</p> <p>21 Q. And is that because too many large or</p> <p>22 bulky substituents would be more likely to result in</p> | Page 71 | <p>1 that says, "The term 'optionally substituted' or</p> <p>2 'substituted' means the referenced group may be</p> <p>3 substituted with one or more additional groups</p> <p>4 individually and independently selected from," and</p> <p>5 then it lists 21 categories of substitutions, right?</p> <p>6 A. Yes, I do.</p> <p>7 Q. So this paragraph provides the definition</p> <p>8 for the claimed term "optionally substituted," right?</p> <p>9 A. Yes.</p> <p>10 Q. And it lists 21 categories of exemplary</p> <p>11 substitutions, right?</p> <p>12 A. I haven't counted them, but I'll --</p> <p>13 Q. I'll represent to you that it's 21</p> <p>14 categories. But you agree --</p> <p>15 A. I'll take your word for it.</p> <p>16 Q. Okay. But you agree that the categories</p> <p>17 listed are exemplary substitutions, right?</p> <p>18 MS. DANEK: Objection, form.</p> <p>19 THE WITNESS: Can you state what you mean</p> <p>20 by exemplary substitutions?</p> <p>21 BY MS. PATEL:</p> <p>22 Q. That these categories are examples of --</p> | Page 73 |

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| <p>1 provide examples of categories of substitutions that<br/>2 are possible for the inhibitors claimed in the<br/>3 challenged claims.<br/>4 MS. DANEK: Objection, form.<br/>5 THE WITNESS: Okay.<br/>6 BY MS. PATEL:<br/>7 Q. Do you agree they provide categories of<br/>8 exemplary substitutions?<br/>9 MS. DANEK: Objection, form.<br/>10 THE WITNESS: My understanding is that<br/>11 those are representative types of substituents that<br/>12 can be introduced to --<br/>13 BY MS. PATEL:<br/>14 Q. That can be introduced to what?<br/>15 A. That can be introduced to a molecule.<br/>16 Q. Do you understand that those are<br/>17 representative types of substituents that can be<br/>18 introduced to the claimed molecules?<br/>19 A. Yes.<br/>20 Q. Does methyl fall into one of these<br/>21 categories?<br/>22 A. I would understand methyl to be alkyl.</p> | Page 74 | <p>1 A. An amino group with large substituents<br/>2 could be considered bulky.<br/>3 Q. You agree that a primary amino group would<br/>4 have a low molecular weight?<br/>5 A. Yes.<br/>6 Q. And you agree that hydroxyl group would<br/>7 fall into one of these categories as well?<br/>8 A. One of the categories is hydroxy.<br/>9 Q. So yes, right?<br/>10 A. I would understand hydroxy to be<br/>11 equivalent to hydroxyl.<br/>12 Q. Would you consider it to be a bulky<br/>13 substitution?<br/>14 A. Not compared to some other substituents.<br/>15 Q. Do you agree that it has a low molecular<br/>16 weight?<br/>17 A. It depends how you define low, but it has<br/>18 a molecular weight of less than 20.<br/>19 Q. Is fluorine one of the groups that are<br/>20 listed in the specification?<br/>21 A. I don't see fluorine specifically listed.<br/>22 Q. Would a POSA consider fluorine to be a</p> | Page 76 |
| <p>1 Q. So yes, right?<br/>2 A. Yes.<br/>3 Q. Do you consider methyl to be a bulky<br/>4 substitution?<br/>5 A. No.<br/>6 Q. Do you agree that methyl has a relatively<br/>7 low molecular weight?<br/>8 MS. DANEK: Objection, form.<br/>9 THE WITNESS: Methyl has a low molecular<br/>10 weight.<br/>11 BY MS. PATEL:<br/>12 Q. And an amino group would also fall into<br/>13 these categories, right? One of these categories?<br/>14 A. An amino is listed as a category.<br/>15 Q. Right. And do you agree that an amino<br/>16 group is not a bulky substitution?<br/>17 MS. DANEK: Objection, form.<br/>18 THE WITNESS: If by amino we're talking<br/>19 about a primary amino group, then that's not bulky.<br/>20 BY MS. PATEL:<br/>21 Q. Would you consider any amino group to be<br/>22 bulky?</p>                                                                     | Page 75 | <p>1 potential optional substitution that could be added<br/>2 to Z prime?<br/>3 A. Yes. Also we would consider fluorine to<br/>4 be a halo substituent.<br/>5 Q. Would they consider it to be a bulky<br/>6 substitution?<br/>7 A. No.<br/>8 Q. Would a POSA consider fluorine to have a<br/>9 low molecular weight?<br/>10 A. Fluorine has a molecular weight of less<br/>11 than 20.<br/>12 Q. And cyanide is a substitution that falls<br/>13 into one of the categories listed, right?<br/>14 A. Cyanide would fall under cyan.<br/>15 Q. So yes?<br/>16 A. Yes.<br/>17 Q. And would a POSA consider that to be a<br/>18 bulky substitution?<br/>19 A. Generally, no.<br/>20 Q. And the methoxy group, that's a<br/>21 substitution that also falls into one of the<br/>22 categories listed, right?</p>                                                                                                            | Page 77 |

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| <p>1 A. Methoxy would fall under alkoxy.</p> <p>2 Q. So yes, right?</p> <p>3 A. Yes.</p> <p>4 Q. Would a POSA consider that to be a bulky</p> <p>5 substitution?</p> <p>6 A. It would depend on the context.</p> <p>7 Q. Would a POSA consider methoxy to be a</p> <p>8 bulky substitution to add to Z prime?</p> <p>9 A. Again, it would depend on the context.</p> <p>10 Q. What further context would you need?</p> <p>11 A. The context of how the molecule was</p> <p>12 binding to its target.</p> <p>13 Q. Okay. So it could potentially be a viable</p> <p>14 optional substitution on Z prime. It just depends on</p> <p>15 the molecule, is that right?</p> <p>16 A. Yes.</p> <p>17 Q. What about fluoromethyl. Is that a</p> <p>18 substitution that falls within one of the categories</p> <p>19 listed?</p> <p>20 A. Yes, fluoromethyl would fall under</p> <p>21 fluoroalkyl.</p> <p>22 Q. Would a POSA consider that to be a bulky</p>                                | Page 78 | <p>1 Q. Would a POSA consider hydrogen to be a</p> <p>2 potential optional substitute to Z prime?</p> <p>3 MS. DANEK: Objection, form.</p> <p>4 THE WITNESS: It's not on the list of</p> <p>5 groups listed here.</p> <p>6 BY MS. PATEL:</p> <p>7 Q. But would a POSA consider it as an</p> <p>8 optional substitution?</p> <p>9 MS. DANEK: Objection, form.</p> <p>10 THE WITNESS: I don't think a POSA would</p> <p>11 consider hydrogen as a substituent.</p> <p>12 BY MS. PATEL:</p> <p>13 Q. Why not?</p> <p>14 A. It depends how you define substituent. If</p> <p>15 -- substituent usually refers to an atom other than</p> <p>16 hydrogen in the way that chemists talk about</p> <p>17 substituents.</p> <p>18 Q. Okay. So -- but there could be hydrogen</p> <p>19 molecules at various positions on the ring, right?</p> <p>20 MS. DANEK: Objection, form.</p> <p>21 THE WITNESS: Yes.</p> <p>22 BY MS. PATEL:</p>                                                                                | Page 80 |
| <p>1 substitution?</p> <p>2 A. Again, it depends on the context.</p> <p>3 Q. So it could potentially be a viable</p> <p>4 optional substitution on Z prime, but it would depend</p> <p>5 on the molecule, right?</p> <p>6 A. That seems fair.</p> <p>7 Q. Okay. And hydrogen certainly falls within</p> <p>8 one of the categories listed here, right?</p> <p>9 A. I don't see --</p> <p>10 Q. Yeah, actually strike that. Hydrogen --</p> <p>11 A. Could you repeat your question?</p> <p>12 Q. Sure. Hydrogen would be a potential</p> <p>13 optional substitution that a POSA would consider for</p> <p>14 Z prime, right?</p> <p>15 A. I'm sorry, can you repeat that?</p> <p>16 Q. Would a POSA consider hydrogen to be a</p> <p>17 potential optional substitution that could be added</p> <p>18 to Z prime?</p> <p>19 MS. DANEK: Objection, form.</p> <p>20 THE WITNESS: I'm not sure what you mean</p> <p>21 by adding hydrogen as a substitute.</p> <p>22 BY MS. PATEL:</p> | Page 79 | <p>1 Q. And vinyl, that is an optional</p> <p>2 substitution that falls within the alkyl group that's</p> <p>3 listed here, right?</p> <p>4 A. Can you point me to the definition of</p> <p>5 alkyl?</p> <p>6 Q. Do you see where it says, "One or more</p> <p>7 additional groups individually or independently</p> <p>8 selected from alkyl"?</p> <p>9 A. I see that you have a definition of alkyl</p> <p>10 for this context.</p> <p>11 Q. Do you think that vinyl wouldn't</p> <p>12 include -- wouldn't be included in the definition of</p> <p>13 alkyl?</p> <p>14 A. It might be, but I'd like to see the</p> <p>15 definition before stating an opinion.</p> <p>16 Q. And if there isn't a definition in the</p> <p>17 patent, what definition would you apply?</p> <p>18 A. I don't know.</p> <p>19 Q. You don't know the definition of alkyl?</p> <p>20 Look at column 12, line 50.</p> <p>21 THE REPORTER: I'm sorry, I didn't hear an</p> <p>22 answer to that question, "You don't know the</p> | Page 81 |

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| <p>1 definition of alkyl?"</p> <p>2 THE WITNESS: I didn't answer that</p> <p>3 question.</p> <p>4 BY MS. PATEL:</p> <p>5 Q. Okay. Why don't you go ahead and answer</p> <p>6 that question.</p> <p>7 A. Okay. I see the definition of alkyl and</p> <p>8 it does include alkene, which wouldn't mean that the</p> <p>9 vinyl that you're mentioning would be an alkyl.</p> <p>10 BY MS. PATEL:</p> <p>11 Q. You're saying it would be or would not</p> <p>12 with?</p> <p>13 A. It would fall under alkyl by this</p> <p>14 definition.</p> <p>15 Q. Okay. Just so the record is clear, you</p> <p>16 agree that a vinyl substitution would fall under the</p> <p>17 definition of alkyl --</p> <p>18 A. Yes.</p> <p>19 Q. -- listed in the specification.</p> <p>20 Okay. What about CH<sub>2</sub>NH<sub>2</sub>. Would that fall</p> <p>21 into one of the categories listed?</p> <p>22 A. Based on that list of 21 terms, I'm not</p>                                                                                    | <p>Page 82</p> <p>1 molecule itself?</p> <p>2 MS. DANEK: Objection, form.</p> <p>3 THE WITNESS: As I said, I don't have</p> <p>4 enough information in this paragraph to determine.</p> <p>5 BY MS. PATEL:</p> <p>6 Q. Right. But I'm asking you something</p> <p>7 different. I'm asking you if -- I'm asking you that</p> <p>8 would a POSA consider CH<sub>2</sub>NH<sub>2</sub> to be too bulky of a</p> <p>9 substitution for Z prime?</p> <p>10 MS. DANEK: Objection, form.</p> <p>11 THE WITNESS: It would depend on the</p> <p>12 context.</p> <p>13 BY MS. PATEL:</p> <p>14 Q. So it could be a viable optional</p> <p>15 substitution, right?</p> <p>16 A. It's possible.</p> <p>17 Q. And formaldehyde, that's a substitution</p> <p>18 that falls within one of the categories listed,</p> <p>19 right?</p> <p>20 A. I don't know. I don't know if</p> <p>21 formaldehyde falls into one of these categories.</p> <p>22 Q. Could it be an acyl?</p>                                                                            |
| <p>1 sure.</p> <p>2 Q. Would it be an amino?</p> <p>3 A. I would want to check the definition of</p> <p>4 amino in this context.</p> <p>5 Q. Or an alkyl?</p> <p>6 A. Based on that paragraph, I don't think I</p> <p>7 have enough information.</p> <p>8 Q. Okay. And jumping back to vinyl, would a</p> <p>9 POSA consider vinyl to be a bulky substitution?</p> <p>10 A. It would depend on the context.</p> <p>11 Q. Okay. So again, this is one of those</p> <p>12 situations that -- where vinyl could be an optional</p> <p>13 substitution on Z prime, but it would depend on the</p> <p>14 particular compound, right?</p> <p>15 MS. DANEK: Objection, form.</p> <p>16 THE WITNESS: It could be a substituent.</p> <p>17 BY MS. PATEL:</p> <p>18 Q. Okay. And would a POSA consider CH<sub>2</sub>NH<sub>2</sub> to</p> <p>19 be a bulky substitution?</p> <p>20 A. It would depend on the context.</p> <p>21 Q. Okay. So it could be an optional</p> <p>22 substitution on Z prime, but it would depend on the</p> | <p>Page 83</p> <p>1 A. I saw the definition of acyl above and the</p> <p>2 definition of that is COR. So it would depend on</p> <p>3 what R was.</p> <p>4 Q. Okay. Would a POSA consider formaldehyde</p> <p>5 as a potential optional substitution on Z prime?</p> <p>6 MS. DANEK: Objection, form.</p> <p>7 THE WITNESS: For it to be an optional</p> <p>8 substituent, it would have to be within these</p> <p>9 categories, is that correct? And I'm not sure it is.</p> <p>10 BY MS. PATEL:</p> <p>11 Q. Outside of these categories, do you think</p> <p>12 a POSA would consider a non-bulky substitution to be</p> <p>13 a potential viable substitution for Z prime?</p> <p>14 MS. DANEK: Objection, form.</p> <p>15 THE WITNESS: In designing kinase</p> <p>16 inhibitors, of course I would consider a number of</p> <p>17 substituents.</p> <p>18 BY MS. PATEL:</p> <p>19 Q. Okay. And would formaldehyde be one of</p> <p>20 them?</p> <p>21 MS. DANEK: Objection, form.</p> <p>22 THE WITNESS: In my experience, I don't</p> |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <p>Page 84</p> <p>Page 85</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |

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| <p>1 remember introducing a formaldehyde group as a</p> <p>2 substituent kinase inhibitor.</p> <p>3 BY MS. PATEL:</p> <p>4 Q. Okay. Is it possible?</p> <p>5 A. Is it possible to introduce a formaldehyde</p> <p>6 substituent? It is possible to introduce a</p> <p>7 formaldehyde substituent, yes.</p> <p>8 Q. Would a POSA consider that to be a bulky</p> <p>9 substitution?</p> <p>10 MS. DANEK: Objection, form.</p> <p>11 THE WITNESS: It would depend on the</p> <p>12 context.</p> <p>13 BY MS. PATEL:</p> <p>14 Q. So it might not be a bulky substitution</p> <p>15 for certain compounds, right?</p> <p>16 A. It would depend on the context.</p> <p>17 Q. What context would it depend on?</p> <p>18 A. How the compound was binding to the</p> <p>19 target.</p> <p>20 Q. So it would depend on the specific</p> <p>21 compound --</p> <p>22 A. And also -- sorry.</p> | <p>Page 86</p> <p>1 compound at issue, right?</p> <p>2 A. It would depend on how the compound was</p> <p>3 binding to its target.</p> <p>4 Q. Which depends on the specific compound at</p> <p>5 issue, right?</p> <p>6 A. Yes.</p> <p>7 Q. So back to the patent, that same paragraph</p> <p>8 we were just looking at, do you see where it says,</p> <p>9 "By way of example an optional substituent may be</p> <p>10 LSRS, wherein each LS is independently selected from</p> <p>11 a bond," and then it lists 15 possible moieties for</p> <p>12 LS into the top of the next column, right?</p> <p>13 A. Yes.</p> <p>14 Q. And then at column 20, line 5, it says</p> <p>15 that each RS is independently selected from, and then</p> <p>16 it lists five different moieties, right?</p> <p>17 A. I don't see what you're referring to. Can</p> <p>18 you repeat that?</p> <p>19 Q. Yeah. If you look at column 20, line 5,</p> <p>20 do you see where it says, "Each RS is independently</p> <p>21 selected from"?</p> <p>22 A. Oh, yes.</p> <p>Page 88</p> |
| <p>1 Q. So it would depend on the specific</p> <p>2 compound itself, right?</p> <p>3 A. Yes.</p> <p>4 Q. What about formamide. Is that a</p> <p>5 substitution that falls within one of the categories</p> <p>6 listed in the specification?</p> <p>7 A. I don't see formamide listed.</p> <p>8 Q. Could it be an acyl or amino?</p> <p>9 A. I don't know.</p> <p>10 Q. Is it possible to introduce a formamide</p> <p>11 substituent?</p> <p>12 MS. DANEK: Objection, form.</p> <p>13 THE WITNESS: That would depend on the</p> <p>14 context.</p> <p>15 BY MS. PATEL:</p> <p>16 Q. So it would depend on the specific</p> <p>17 compound itself, right?</p> <p>18 A. Yes.</p> <p>19 Q. And would a POSA consider it to be a bulky</p> <p>20 substitution?</p> <p>21 A. That would depend on the specific context.</p> <p>22 Q. So it would depend on the specific</p>                | <p>Page 87</p> <p>1 Q. And then it lists five different moieties?</p> <p>2 A. Okay.</p> <p>3 Q. Do you see that?</p> <p>4 A. Yes.</p> <p>5 Q. So LSRS are all examples the specification</p> <p>6 provides when defining the term "optional</p> <p>7 substitution," right?</p> <p>8 A. Yes.</p> <p>9 Q. Do you agree that some of these exemplary</p> <p>10 moieties would be very bulky if added to Z prime?</p> <p>11 MS. DANEK: Objection, form.</p> <p>12 THE WITNESS: There are no specific</p> <p>13 moieties. So I can't give a simple answer to that</p> <p>14 question.</p> <p>15 BY MS. PATEL:</p> <p>16 Q. You understand the formula, though, right,</p> <p>17 LSRS where LS is independently selected from 15</p> <p>18 possible moieties and RS is independently selected</p> <p>19 from five possible moieties?</p> <p>20 A. Yes.</p> <p>21 Q. Okay. So there's a large number of</p> <p>22 combinations there, right?</p> <p>Page 89</p>                                                                                                         |

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| <p>1 MS. DANEK: Objection, form.</p> <p>2 THE WITNESS: There are a list of</p> <p>3 possibilities.</p> <p>4 BY MS. PATEL:</p> <p>5 Q. So are there any possibilities of LSRS</p> <p>6 substitutions that you think would be particularly</p> <p>7 bulky as a Z prime substitution?</p> <p>8 MS. DANEK: Objection, form.</p> <p>9 THE WITNESS: I'm sorry, can you repeat</p> <p>10 that question again?</p> <p>11 BY MS. PATEL:</p> <p>12 Q. Based on the definition of LS and RS, are</p> <p>13 there any exemplary optional substitutions that you</p> <p>14 would consider to be bulky?</p> <p>15 A. It would depend on the context.</p> <p>16 Q. So with regard to all of the exemplary</p> <p>17 optional substitutions listed as LSRS, are you saying</p> <p>18 it would depend on the context whether or not a POSA</p> <p>19 would consider them to be bulky?</p> <p>20 A. If a POSA had defined bulky simply to</p> <p>21 refer to size, then some of these groups are larger</p> <p>22 than others.</p> | <p>Page 90</p> | <p>1 feel confident expressing an opinion at the moment.</p> <p>2 Q. But when drafting your declaration, you</p> <p>3 did look at this paragraph of the specification,</p> <p>4 right?</p> <p>5 A. I don't remember specifically looking at</p> <p>6 this paragraph.</p> <p>7 Q. Is it your view that any of these LSRS</p> <p>8 optional substitutions listed would not work?</p> <p>9 MS. DANEK: Objection, form.</p> <p>10 THE WITNESS: I've not seen any evidence</p> <p>11 that they wouldn't.</p> <p>12 BY MS. PATEL:</p> <p>13 Q. And you agree that the specification</p> <p>14 provides these as exemplary optional substitutions</p> <p>15 for the claimed molecules, right?</p> <p>16 A. Yes.</p> <p>17 Q. Does the definition reference Lipinski's</p> <p>18 rules?</p> <p>19 MS. DANEK: Objection, form.</p> <p>20 THE WITNESS: Which definition?</p> <p>21 BY MS. PATEL:</p> <p>22 Q. Let me rephrase, yeah.</p> | <p>Page 92</p> |
| <p>1 Q. So would a POSA not use some of those</p> <p>2 groups that you consider larger than others?</p> <p>3 MS. DANEK: Objection, form.</p> <p>4 THE WITNESS: I don't know.</p> <p>5 BY MS. PATEL:</p> <p>6 Q. Would a POSA potentially use every one of</p> <p>7 these LSRS exemplary substitutions listed?</p> <p>8 MS. DANEK: Objection, form.</p> <p>9 THE WITNESS: I don't know.</p> <p>10 BY MS. PATEL:</p> <p>11 Q. Why don't you know?</p> <p>12 A. A POSA would choose specific substituents</p> <p>13 for a specific reason and that would depend on the</p> <p>14 context of the molecule in question.</p> <p>15 Q. But is it your view that any one of these</p> <p>16 could potentially work?</p> <p>17 MS. DANEK: Objection, form.</p> <p>18 BY MS. PATEL:</p> <p>19 Q. And let me just repeat my question. Is it</p> <p>20 your view that any one of these could potentially</p> <p>21 work?</p> <p>22 A. I haven't fully considered that. I don't</p>                                           | <p>Page 91</p> | <p>1 Does the definition of optional</p> <p>2 substitution provided in the specification reference</p> <p>3 Lipinski's rules?</p> <p>4 A. I don't see that.</p> <p>5 Q. Are Lipinski's rules referenced anywhere</p> <p>6 in the specification?</p> <p>7 A. I'm not aware of it.</p> <p>8 MS. PATEL: Okay. Why don't we take a</p> <p>9 break.</p> <p>10 THE VIDEOGRAPHER: We are off the record.</p> <p>11 The time is 12:03 p.m.</p> <p>12 (Recess.)</p> <p>13 THE VIDEOGRAPHER: We are back on the</p> <p>14 record. The time is 12:36 p.m.</p> <p>15 BY MS. PATEL:</p> <p>16 Q. Dr. Scott, did you speak with your counsel</p> <p>17 during this or any other breaks today?</p> <p>18 A. We chatted over lunch.</p> <p>19 Q. But you didn't discuss your testimony --</p> <p>20 A. No.</p> <p>21 Q. -- today?</p> <p>22 A. No.</p>                                                                                         | <p>Page 93</p> |

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| <p>1 Q. Okay. Could you please take a look at<br/>2 your declaration, please. And turn to paragraph 32.<br/>3 A. Okay. I'm there.<br/>4 Q. Okay. You state here that "In June 2011,<br/>5 a POSA reading the '803 patent to identify<br/>6 ibrutinib-like irreversible BTKIs for use in the<br/>7 claimed method would have understood that certain<br/>8 physicochemical properties could be calculated and/or<br/>9 predicted from the ibrutinib-like irreversible BTKI's<br/>10 structure," right?<br/>11 A. Yes.<br/>12 Q. And then you state that these<br/>13 physicochemical properties can be calculated in<br/>14 silico using software like ChemDraw, right?<br/>15 A. Yes.<br/>16 Q. In 2011, did you solely rely on such<br/>17 software to predict physicochemical properties of the<br/>18 compound?<br/>19 MS. DANEK: Objection, form.<br/>20 THE WITNESS: No.<br/>21 BY MS. PATEL:<br/>22 Q. What else would you have relied on?</p>                                                                                                       | <p>Page 94</p> <p>1 fact that you had also run in silico testing,<br/>2 correct?<br/>3 MS. DANEK: Objection, form.<br/>4 THE WITNESS: I wouldn't describe it as<br/>5 necessary.<br/>6 BY MS. PATEL:<br/>7 Q. So why did you do it?<br/>8 A. At times it was useful to establish how<br/>9 accurate the predictions were.<br/>10 Q. Are there times where you would only use<br/>11 in silico testing to determine physicochemical<br/>12 properties and not run any experiments afterwards to<br/>13 establish how accurate the predictions were?<br/>14 A. If we're talking about the example of<br/>15 lipophilicity, I think it's fair that we didn't<br/>16 generate experimental data on every compound.<br/>17 Q. And when you were talking about<br/>18 AstraZeneca's proprietary software, that wouldn't<br/>19 have been software that would be considered an<br/>20 industry standard drawing package or ChemDraw, right?<br/>21 A. My understanding is that different<br/>22 companies might have their own software and my</p> <p>Page 96</p> |
| <p>1 A. At the time, AstraZeneca had a proprietary<br/>2 program that predicted or calculated some of these<br/>3 properties.<br/>4 Q. When you say proprietary program, are you<br/>5 talking about a software?<br/>6 A. A software program that had been developed<br/>7 internally.<br/>8 Q. Okay. And did you still run experiments<br/>9 to determine physicochemical properties of the<br/>10 compounds even after in silico testing?<br/>11 A. Based on that list of physicochemical<br/>12 properties starting on the last line of page 18, most<br/>13 of those would simply have been calculated. We<br/>14 wouldn't have run an experiment to measure molecular<br/>15 weight. That's just a characteristic of a compound<br/>16 that can be calculated. We may have had an assay<br/>17 that measured lipophilicity.<br/>18 Q. And is that to confirm that the in silico<br/>19 testing was accurate?<br/>20 A. The assay was to generate the data that we<br/>21 wanted.<br/>22 Q. And the assay was necessary despite the</p> <p>Page 95</p> | <p>1 understanding is that these would be generally quite<br/>2 similar.<br/>3 Q. Would the accuracy of predictive value of<br/>4 each of these softwares differ?<br/>5 A. I don't know.<br/>6 Q. If you're using ChemDraw alone to predict<br/>7 physical chemical properties, would you choose to run<br/>8 experiments after that to confirm the accuracy of<br/>9 your results?<br/>10 A. Most of the properties that I would have<br/>11 used ChemDraw to calculate would not have needed<br/>12 confirmation by an experiment such as molecular<br/>13 weight.<br/>14 Q. What other properties?<br/>15 A. Polar surface area, PSA.<br/>16 Q. Anything else?<br/>17 A. ChemDraw would have -- I'd have to check,<br/>18 but my recollection is that ChemDraw can calculate<br/>19 the number of hydrogen bond donors and acceptors.<br/>20 Q. Did you always use software to predict<br/>21 physicochemical properties of compounds that you<br/>22 planned to synthesize?</p> <p>Page 97</p>                                                         |

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| <p>1 A. No.</p> <p>2 Q. When would you not use them, use the</p> <p>3 software?</p> <p>4 A. If I was preparing a compound that was</p> <p>5 structured at least similar to an existing compound,</p> <p>6 I would have inferred that it would have similar</p> <p>7 properties.</p> <p>8 Q. What would you consider similar to an</p> <p>9 existing compound?</p> <p>10 A. That would depend on the individual</p> <p>11 property.</p> <p>12 Q. Which physicochemical properties would</p> <p>13 require confirmation through experimentation?</p> <p>14 A. Of the list, I -- we started discussing,</p> <p>15 lipophilicity is the only one that could be -- that</p> <p>16 there's an experiment to measure it.</p> <p>17 Q. And in paragraph 32, you also state that</p> <p>18 "In 2011, it was routine to consider the</p> <p>19 physicochemical properties of compounds to be</p> <p>20 synthesized to help prioritize those with the</p> <p>21 potential for good PK properties."</p> <p>22 Do you see that?</p> | <p>Page 98</p> <p>1 overall target profile that compounds is hoping -- or</p> <p>2 hoping to meet.</p> <p>3 Q. And would physicochemical properties be</p> <p>4 one of those -- be part of that profile?</p> <p>5 A. Physicochemical properties would be</p> <p>6 considered as part of the overall desired profile.</p> <p>7 Q. But it would be more of a weighing, not --</p> <p>8 A. Correct. Yes.</p> <p>9 THE REPORTER: I'm sorry, I didn't</p> <p>10 understand that question. "It would be more of a" --</p> <p>11 BY MS. PATEL:</p> <p>12 Q. Yeah. You would consider physicochemical</p> <p>13 properties but would not exclude a compound simply</p> <p>14 because it didn't have good physicochemical</p> <p>15 properties, right?</p> <p>16 A. We wouldn't use any single parameter to</p> <p>17 rule out a compound.</p> <p>18 Q. So what are some other factors that go</p> <p>19 into the target profile?</p> <p>20 A. In the case of the kinase project I</p> <p>21 mentioned earlier, we were looking to demonstrate</p> <p>22 activity in an animal model.</p> <p>Page 100</p> |
| <p>1 A. Yes.</p> <p>2 Q. Okay. Would you at that time have only</p> <p>3 synthesized compounds that the software predicted to</p> <p>4 have good physicochemical properties?</p> <p>5 A. No.</p> <p>6 Q. Why not?</p> <p>7 A. There can be good reasons to make</p> <p>8 compounds that are outside of the Lipinski</p> <p>9 guidelines.</p> <p>10 Q. What are some of those reasons?</p> <p>11 A. You might want to test whether you can</p> <p>12 pick up an additional binding interaction.</p> <p>13 Q. Any other reasons?</p> <p>14 MS. DANEK: I don't believe they heard</p> <p>15 you.</p> <p>16 THE WITNESS: I can't think of any others</p> <p>17 off the top of my head right now.</p> <p>18 BY MS. PATEL:</p> <p>19 Q. So what considerations go into deciding</p> <p>20 which compounds you would synthesize?</p> <p>21 A. Each drug discovery project for -- for</p> <p>22 example, a kinase inhibitor project will have an</p> <p>Page 99</p>                                                            | <p>1 Q. And so for that you would need to have</p> <p>2 synthesized the compound, right?</p> <p>3 A. Yes.</p> <p>4 Q. And when you say it was routine to</p> <p>5 consider the physicochemical properties of the</p> <p>6 compounds to be synthesized, do you mean that it was</p> <p>7 routine to do so in the context of drug design?</p> <p>8 A. If by drug design you mean the design of</p> <p>9 target compounds for a drug discovery project, then</p> <p>10 yes.</p> <p>11 Q. What is the goal of a drug discovery</p> <p>12 project?</p> <p>13 A. To develop a new therapeutic agent.</p> <p>14 Q. So in a drug discovery project, you have a</p> <p>15 certain number of potential candidates and the goal</p> <p>16 is to determine which of those is likely to be the</p> <p>17 best therapeutic, is that right?</p> <p>18 A. The goal is to identify a compound that is</p> <p>19 good enough to take into the clinic with an</p> <p>20 expectation of success.</p> <p>21 Q. And do you usually start that project out</p> <p>22 with a series of candidates?</p> <p>Page 101</p>   |

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| <p>1 A. So "candidate" has a specific meaning in<br/>2 drug discovery. So I'd like to be clear on what you<br/>3 mean here.<br/>4 Q. What meaning does it have in the context<br/>5 of drug discovery?<br/>6 A. My understanding is it would refer to a<br/>7 compound that had progressed into late stage<br/>8 development.<br/>9 Q. And what about compounds that were still<br/>10 in the early stage of development. Would that just<br/>11 be considered a series?<br/>12 A. We would call those compounds.<br/>13 Q. Okay. So say that you did not prioritize<br/>14 a particular compound or did not advance a particular<br/>15 compound. Would that mean that that compound does<br/>16 not work at all to inhibit the target?<br/>17 A. No.<br/>18 Q. Okay. Why?<br/>19 A. At each stage of the drug discovery<br/>20 process, we would prioritize the most promising<br/>21 compounds in alignment with the resources available.<br/>22 Q. So wouldn't necessarily mean that the</p>                                                                                                     | <p>Page 102</p> <p>1 A. I can't think of a specific example right<br/>2 now.<br/>3 Q. Have you ever prioritized a compound<br/>4 because the physicochemical properties indicated it<br/>5 would have good PK properties only to later find out<br/>6 that the PK properties were very bad?<br/>7 A. Again, in the example of CSF-1R, we had a<br/>8 number of compounds that we were interested in<br/>9 pursuing where the PK profile was not good enough for<br/>10 that project.<br/>11 Q. In that situation, did the physicochemical<br/>12 properties indicate that the PK profile might have<br/>13 been good enough?<br/>14 A. I don't remember specific details, but we<br/>15 would look at the overall physicochemical properties<br/>16 to help prioritize the compounds that we felt had the<br/>17 best chance of success. There were examples in<br/>18 CSF-1R where compounds didn't have the PK that we<br/>19 hoped that they would for that project.<br/>20 Q. In that last part, you said there were<br/>21 examples in the CSF-1R project where compounds didn't<br/>22 have the PK that we originally hoped for that</p> <p>Page 104</p> |
| <p>1 deprioritized candidate would have bad PK properties,<br/>2 right, for example? Or, you know, I used a word that<br/>3 you didn't like, so let me rephrase it.<br/>4 That wouldn't necessarily mean that the<br/>5 deprioritized compound would have, for example, bad<br/>6 PK properties.<br/>7 A. I'm sorry, maybe you could rephrase the<br/>8 question. Are you saying that we might deprioritize<br/>9 compounds that had bad PK?<br/>10 Q. I'm saying that if a compound was<br/>11 deprioritized, it wouldn't necessarily mean that it<br/>12 had bad PK, just that it wasn't as promising as the<br/>13 prioritized compounds, right?<br/>14 A. There are different reasons to prioritize<br/>15 one compound over another and it --<br/>16 Q. That's one example, right?<br/>17 A. In the kinase projects I worked on, we<br/>18 looked at PK as one of the parameters used to<br/>19 prioritize compounds.<br/>20 Q. Have you ever deprioritized a compound<br/>21 because the physicochemical properties indicated that<br/>22 it would have bad PK properties?</p> <p>Page 103</p> | <p>1 project, is that right?<br/>2 A. Yes.<br/>3 Q. Can you turn to paragraph 36, please. So<br/>4 you state there that "In considering Z prime<br/>5 scaffolds for use in the compounds of the '803 patent<br/>6 claims, a POSA would have been aware of available<br/>7 tools to assess ADME-related characteristics of<br/>8 ATP-competitive protein kinase inhibitors to evaluate<br/>9 candidate ibrutinib-like irreversible BTKIs."<br/>10 Do you see that?<br/>11 A. Yes.<br/>12 Q. ADME stands for absorption, distribution,<br/>13 metabolism and excretion, right?<br/>14 A. Yes.<br/>15 Q. Those are PK parameters?<br/>16 A. Yes.<br/>17 Q. You state here that "A POSA would have a<br/>18 toolbox of diverse in vitro ADME technologies to<br/>19 predict PK parameters of an inhibitor," right?<br/>20 A. Yes.<br/>21 Q. You state that "To address absorption in<br/>22 particular, scientists were advised to embrace a</p> <p>Page 105</p>                                                                                                                                                                                                   |

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| <p>1 whole set of models and methods that determine</p> <p>2 solubility, lipophilicity, ionization, permeability,</p> <p>3 and the interaction with transporters," right?</p> <p>4 A. Yes.</p> <p>5 Q. And the only reference you cite in this</p> <p>6 paragraph to support your opinions is Exhibit 2040,</p> <p>7 right?</p> <p>8 A. Correct.</p> <p>9 Q. Specifically, pages 15, 38 through 46 and</p> <p>10 table 1.2, right?</p> <p>11 A. Yes.</p> <p>12 Q. So can you pull up Exhibit 2040,</p> <p>13 Dr. Scott?</p> <p>14 A. Okay. I have it.</p> <p>15 (Exhibit No. 2040 was identified for</p> <p>16 the record.)</p> <p>17 BY MS. PATEL:</p> <p>18 Q. So this is Exhibit 2040 that you cite in</p> <p>19 paragraph 36 of your declaration, right?</p> <p>20 A. Yes.</p> <p>21 Q. And it's an excerpt from a book titled</p> <p>22 Protein Kinases As Drug Targets, right?</p> | Page 106 | <p>1 the last paragraph on that page. So in that</p> <p>2 paragraph, the introduction explains that chapter 1</p> <p>3 describes a selection of in vitro assays that are</p> <p>4 critical for the optimization process of</p> <p>5 small-molecule kinase inhibitors, right?</p> <p>6 A. Okay.</p> <p>7 Q. Do you see that?</p> <p>8 A. I see that.</p> <p>9 Q. What does optimization process refer to?</p> <p>10 A. I would understand that to mean the</p> <p>11 improvement of certain compound parameters.</p> <p>12 Q. And it would mean improvement over what?</p> <p>13 A. Over the early compounds.</p> <p>14 Q. So it involves a process of identifying</p> <p>15 the most promising kinase inhibitors in a series that</p> <p>16 have optimal characteristics, is that right?</p> <p>17 A. It refers, I think, to an iterative</p> <p>18 process of testing and design and preparation of</p> <p>19 additional compounds.</p> <p>20 Q. And for what purpose is that?</p> <p>21 A. One purpose might be to design more potent</p> <p>22 compounds.</p> | Page 108 |
| <p>1 A. Yes.</p> <p>2 Q. And it was published in 2011?</p> <p>3 A. Yes.</p> <p>4 Q. Can you go to page 15. And when I say</p> <p>5 page 15, what I mean, you know, the stamped Exhibit</p> <p>6 2040.015.</p> <p>7 A. The introduction page?</p> <p>8 Q. Correct.</p> <p>9 A. Yes. Okay. I'm there.</p> <p>10 Q. So this is the beginning of chapter 1 of</p> <p>11 the book, right?</p> <p>12 A. I believe so, yes.</p> <p>13 Q. And that chapter is titled In Vitro</p> <p>14 Characterization of Small-Molecule Kinase Inhibitors?</p> <p>15 A. Yes.</p> <p>16 Q. The page contains section 1.1 of chapter</p> <p>17 1, right?</p> <p>18 A. Yes.</p> <p>19 Q. Like you said, that's the introduction,</p> <p>20 right?</p> <p>21 A. Yes.</p> <p>22 Q. Okay. So can you look -- take a look at</p>                                                                                     | Page 107 | <p>1 Q. And then this paragraph also states that</p> <p>2 "One needs to consider the mode of inhibition and</p> <p>3 should be prepared for unexpected exceptions from the</p> <p>4 general rules," right?</p> <p>5 A. I see that.</p> <p>6 Q. What are the general rules that this</p> <p>7 statement is referring to?</p> <p>8 A. I don't know.</p> <p>9 Q. But you relied on this page to support</p> <p>10 your opinions in paragraph 36, right?</p> <p>11 A. This reference contains a discussion of</p> <p>12 kinase enzyme assays and also in vitro ADME assays,</p> <p>13 and I relied on this reference to support my opinion</p> <p>14 about the in vitro ADME assays that were available.</p> <p>15 Q. And in your opinion, this statement</p> <p>16 doesn't refer to the ADME assays?</p> <p>17 MS. DANEK: Objection, form.</p> <p>18 THE WITNESS: Reading in here, I think it</p> <p>19 refers to the biochemical enzyme assay.</p> <p>20 BY MS. PATEL:</p> <p>21 Q. Can you turn to page 38.</p> <p>22 A. Okay. I'm at page 38.</p>                | Page 109 |

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| <p>1 Q. This page is the beginning of section 1.1<br/>2 of chapter 1, right?<br/>3 A. I'm sorry, can you repeat that?<br/>4 Q. This page is the beginning of section 1.4<br/>5 of chapter 1, right?<br/>6 A. Yes.<br/>7 Q. And it's titled Addressing ADME Issues of<br/>8 Protein Kinase Inhibitors in Early Drug Discovery?<br/>9 A. Yes.<br/>10 Q. Do you see there where the introduction<br/>11 begins, "Ideally, the optimization process of<br/>12 potential hits to leads and finally to candidates for<br/>13 preclinical and clinical trials should be guided not<br/>14 only by good PD parameters but also by satisfactory<br/>15 PK parameters to avoid attrition during drug<br/>16 development"?<br/>17 Do you see that?<br/>18 MS. DANEK: Object to form.<br/>19 THE WITNESS: I see that.<br/>20 BY MS. PATEL:<br/>21 Q. What does optimization process of<br/>22 potential hits to leads refer to?</p>                                                                                                                                                 | <p>Page 110</p> <p>1 of the compound collection that we believed had a<br/>2 good chance of activity against the new kinase.<br/>3 Q. And again, that would mean that the<br/>4 compound that -- again, that would mean that the<br/>5 subset that you would screen would have been<br/>6 synthesized and then you would run some assays on<br/>7 those synthesized compounds, right?<br/>8 A. Correct. We would do an initial round of<br/>9 biochemical testing.<br/>10 Q. And then the statement we were just<br/>11 looking at, it also says -- it says, "Ideally, the<br/>12 optimization process of potential hits to leads and<br/>13 finally to candidates for preclinical and clinical<br/>14 trials should be guided by PD and PK parameters."<br/>15 So even after the leads are identified,<br/>16 there would be some preclinical and clinical testing<br/>17 that's needed, right?<br/>18 A. Yes, that's correct.<br/>19 Q. And then do you see the last sentence of<br/>20 the first paragraph there?<br/>21 A. The one starting, "Mainly"?<br/>22 Q. Yes. So it says, "Mainly during the past</p> <p>Page 112</p> |
| <p>1 A. Optimization would refer to the<br/>2 improvement of one or more parameters.<br/>3 Q. And what does it mean -- who does<br/>4 "potential hits to leads" refer to?<br/>5 A. In my experience, a potential hit would be<br/>6 a compound that was found to be active in an initial<br/>7 screening campaign. A lead would be a compound that<br/>8 had some of the desired properties that the project<br/>9 was looking to optimize.<br/>10 Q. What would the initial screening campaign<br/>11 entail?<br/>12 A. It would depend on the particular target.<br/>13 Q. What would the initial screening campaign<br/>14 entail today for assuming BTK is the target?<br/>15 A. I don't know.<br/>16 Q. For any kinase inhibitor project -- sorry.<br/>17 Strike that. Why don't you know?<br/>18 A. I'm not sure there would be a typical<br/>19 screening campaign, was it, for a new BTK project?<br/>20 Q. Screening campaign.<br/>21 A. In my experience at AstraZeneca for a<br/>22 kinase project, we would typically screen the subset</p> <p>Page 111</p> | <p>1 two decades, a toolbox of diverse in vitro ADME<br/>2 technologies has been elaborated that enables<br/>3 scientists to filter promising drug candidates at an<br/>4 early stage of drug discovery when usually a few in<br/>5 vivo data are available."<br/>6 A. Yes, I see that.<br/>7 Q. The toolbox contains in vitro<br/>8 technologies, right?<br/>9 A. Yes, the toolbox is referring to a set of<br/>10 in vitro ADME assays.<br/>11 Q. And it says, "Filtering promising drug<br/>12 candidates," right?<br/>13 A. It does say that, yes.<br/>14 Q. So these tools are helpful for identifying<br/>15 promising candidates, right?<br/>16 A. They're useful in identifying the more<br/>17 promising compounds within the set available.<br/>18 Q. Would they also be useful in identifying<br/>19 compounds that are not likely to work?<br/>20 A. We would use the data to make<br/>21 prioritization decisions on which compounds to<br/>22 progress.</p> <p>Page 113</p>                                                                                                                                         |

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| <p>Page 114</p> <p>1 Q. So it wouldn't -- okay. Just because a<br/>2 compound was not identified as a lead doesn't mean it<br/>3 wouldn't work, though, right?<br/>4 A. Typically throughout drug discovery, we're<br/>5 looking to filter compounds to prioritize ones with<br/>6 the best chance of success at the next stage and<br/>7 ultimately with the best chance of success in the<br/>8 clinic. But we can't be certain that compounds we<br/>9 don't progress would not be successful.<br/>10 Q. Can you turn to page 39, please.<br/>11 A. I'm there.<br/>12 Q. Turn to the third paragraph. It starts<br/>13 with, "This section will give a brief overview of in<br/>14 vitro technologies."<br/>15 Do you see that?<br/>16 A. Yes.<br/>17 Q. Do you see it identifies table 1.2?<br/>18 A. Yes.<br/>19 Q. Which -- you know, table -- and then you<br/>20 see table 1.2 identifies "in vitro technologies that<br/>21 address ADME-related characteristics of<br/>22 ATP-competitive protein kinase inhibitors that are</p> | <p>Page 116</p> <p>1 referring to every single method listed in that<br/>2 column or just the ones listed for absorption<br/>3 solubility?<br/>4 A. I've never directly participated in any of<br/>5 these experiments.<br/>6 Q. Okay.<br/>7 MS. PATEL: Why don't we take a break.<br/>8 THE VIDEOGRAPHER: We are off the record.<br/>9 The time is 1:23 p.m.<br/>10 (Recess.)<br/>11 THE VIDEOGRAPHER: We are back on the<br/>12 record. The time is 1:34 p.m.<br/>13 MS. PATEL: I pass the witness.<br/>14 EXAMINATION BY COUNSEL FOR PATENT OWNER<br/>15 BY MS. DANEK:<br/>16 Q. Dr. Scott, I just have one question.<br/>17 Do you still have in front of you Exhibit<br/>18 2040, the Hafenbradl chapter?<br/>19 A. Yes, I do.<br/>20 Q. And do you recall being asked questions on<br/>21 Exhibit 2040.0039, table 1.2?<br/>22 A. Yes.</p>                                   |
| <p>Page 115</p> <p>1 most relevant for the routine screening of compounds<br/>2 in the drug discovery phase," right?<br/>3 A. Yes.<br/>4 Q. So let's go through these technologies.<br/>5 The first PK parameter listed is absorption and the<br/>6 assay listed for that is a solubility assay, right?<br/>7 A. Yes.<br/>8 Q. And then there's one, two, three -- four<br/>9 methods listed to determine solubility, is that<br/>10 correct?<br/>11 A. That's correct.<br/>12 Q. The first one that's listed is shake<br/>13 flask. What does that entail?<br/>14 A. I'm not familiar with the details of the<br/>15 assay.<br/>16 Q. Are you familiar with any of these that<br/>17 are listed -- any of these methods that are listed to<br/>18 determine solubility?<br/>19 A. I wouldn't know how to conduct the<br/>20 experiment of any of these.<br/>21 Q. And when you say you wouldn't know how to<br/>22 conduct the experiment of any of these, are you</p>                                                                    | <p>Page 117</p> <p>1 Q. And these assays that are listed for ADME<br/>2 in vitro technologies?<br/>3 A. Yes.<br/>4 Q. And I believe you said that you wouldn't<br/>5 know how to conduct the experiments that are listed<br/>6 in this table, is that right?<br/>7 A. That's correct.<br/>8 Q. Do you have any familiarity with the<br/>9 results of the experiments listed in this table? The<br/>10 data generated by the experiments?<br/>11 A. Yes. The majority of these assays were<br/>12 run routinely while I was at AstraZeneca to generate<br/>13 data on multiple compounds.<br/>14 MS. DANEK: I have no further questions.<br/>15 MS. PATEL: I have no further questions.<br/>16 THE VIDEOGRAPHER: We are off the record.<br/>17 The time is 1:35 p.m.<br/>18 (Whereupon, at 1:35 p.m., the taking of<br/>19 the instant deposition ceased.)<br/>20<br/>21<br/>22</p> |

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| <div>1 CERTIFICATE OF REPORTER</div> <div>2 UNITED STATES OF AMERICA ) ss:</div> <div>3 DISTRICT OF COLUMBIA )</div> <div>4 I, MARY GRACE CASTLEBERRY, RPR, the officer</div> <div>5 before whom the foregoing proceedings were taken, do</div> <div>6 hereby certify that the foregoing transcript is a</div> <div>7 true and correct record of the proceedings; that said</div> <div>8 proceedings were taken by me stenographically to the</div> <div>9 best of my ability and thereafter reduced to</div> <div>10 typewriting under my supervision; and that I am</div> <div>11 neither counsel for, related to, nor employed by any</div> <div>12 parties to this case and have no interest, financial</div> <div>13 or otherwise, in its outcome.</div> <div>14</div> <div>15</div> <div>16</div> <div>17 Notary Public in and for</div> <div>18 The District of Columbia</div> <div>19</div> <div>20</div> <div>21 My commission expires: 7/14/2026</div> <div>22</div> | <div>Page 118</div> |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                     |

Notice Date: Monday, 30. September 2024

Attention: David A. Scott

Re:BeiGene USA, Inc. and BeiGene, LTD. v. Pharmacyclics LLC  
Deposition of David A. Scott (9/27/2024)

NOTICE REGARDING SIGNING DEPOSITION TRANSCRIPT

The above referenced transcript is available for review. Within 30 days, or the applicable timeframe of your legal jurisdiction, the witness may read the testimony to verify its accuracy. Any changes can be noted on the following errata page.

Once the transcript has been reviewed, the witness should sign and date the certificate of deponent page. The signed certificate, errata, and original transcript (if provided) must be returned to TP.One per the rules of civil procedure.

If the transcript and errata are not returned within the allotted time, the unsigned transcript may be used as if signed by the witness.

Thank you,

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Deponent Errata Page

Notice Date: 09/30/2024

Deposition Date: 9/27/2024

Deponent: David A. Scott

Case Name: BeiGene USA, Inc. and BeiGene, LTD.  
v. Pharmacyclics LLC

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CERTIFICATE OF DEPONENT

I hereby certify that I have read and examined the foregoing transcript, and the same is a true and accurate record of the testimony given by me. Any additions or corrections that I feel are necessary, I will attach on a separate sheet of paper to the original transcript.

\_\_\_\_\_  
Signature of Deponent

I hereby certify that the individual representing himself/herself to be the above-named individual, appeared before me this \_\_\_\_ day of \_\_\_\_\_, 20\_\_, and executed the above certificate in my presence.

\_\_\_\_\_  
NOTARY PUBLIC IN AND FOR

\_\_\_\_\_  
County Name

MY COMMISSION EXPIRES:

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