Federal Court Cour fédérale

Date: 20250512

Dockets: T-1094-23
T-1095-23

Citation: 2025 FC 754

Ottawa, Ontario, May 12, 2025

PRESENT: The Honourable Madam Justice Furlanetto

BETWEEN:

ALEXION PHARMACEUTICALS, INC. AND ALEXION PHARMA INTERNATIONAL OPERATIONS LIMITED

Plaintiffs

and

AMGEN CANADA INC.

Defendant

PUBLIC JUDGMENT AND REASONS
(Identical to the Confidential Judgment and Reasons issued on April 28, 2025)

I. Overview

[1] This judgment arises from two patent infringement actions brought under subsection 6(1) of the *Patent Medicines (Notice of Compliance Regulations)*, SOR/93-133 [*PMNOC Regulations*]. The patent at issue is Canadian Patent No. 2,645,810 [810 Patent]. The innovative drug relating to the action is SOLIRIS® (eculizumab), which is an intravenously administered

biologic drug that is used to treat patients with paroxysmal nocturnal hemoglobinuria [PNH]; a rare blood disorder that causes the breakdown of red blood cells.

[2] The Plaintiff, Alexion Pharmaceuticals, Inc. [API], is the registered owner of the 810 Patent. The Plaintiff, Alexion Pharma International Operations Limited [APIOL], is the asserted beneficial owner of the 810 Patent. The parties agree that the Plaintiffs [collectively, Alexion] have authority to bring the present action as owners of the patent.

[3] The Defendant, Amgen Canada Inc. [Amgen], seeks to market a proposed eculizumab product, BEKEMV [Amgen Product] in Canada and delivered two Notices of Allegation [NOA] in respect of its New Drug Submission [NDS] filings. The first NOA related to Amgen's NDS No. 263132 and led to T-1094-23. The second NOA related to NDS No. 273714 and led to T-1095-23.

[4] Alexion claims that the making, constructing, using, or selling of the Amgen Product will directly and/or indirectly infringe claims 1 and 2 of the 810 Patent [Asserted Claims].

[5] For purposes of this proceeding, Amgen admits that there will be infringement of the Asserted Claims and relies on its defence that the Asserted Claims are invalid for anticipation and obviousness. The parties agree that the differences between T-1094-23 and T-1095-23, and Amgen's NDS Nos. 263132 and 273714, which were material for infringement, are not relevant to the issue of validity.

[6] For the reasons that follow, I find on the evidence before me that Amgen has not met its burden of establishing that the Asserted Claims are anticipated or obvious. As such, the action is allowed, a declaration of infringement, injunction and delivery up are ordered, and costs awarded.

II. **Background**

[7] The 810 Patent is listed on the Patent Register in association with the medicine eculizumab. Eculizumab is the active ingredient in Alexion's product SOLIRIS®, which has been sold in Canada since 2009. It is the only medicine that has been approved for the treatment of PNH in Canada.

[8] PNH is a rare disease caused by an acquired genetic mutation that makes a person's red blood cells break apart prematurely in a process known as hemolysis. Those patients that have PNH produce red blood cells that lack certain proteins on their cell surface that inhibit the effect of the human complement system (a complex network of proteins triggered in the blood by a series of cascading biochemical reactions as part of the body's immune response to eliminate pathogens).

[9] The human complement system is activated by three pathways, all of which converge and result in the cleavage of complement protein C3 into C3a and C3b, and subsequently the cleavage of complement protein C5 into C5a and C5b. The latter steps lead to the activation of the terminal complement pathway (C5b to C9) responsible for the activation and destruction of target cells.

[10] In a patient with PNH, the proteins triggered by the complement system attack the patient's red blood cells making them sensitive to premature destruction and result in an increase in the release of hemoglobin into the bloodstream.

[11] Eculizumab is a recombinant humanized monoclonal antibody directed against complement protein C5. Eculizumab binds to complement protein C5, preventing its cleavage and the terminal complement pathway from attacking abnormal red blood cells, thereby protecting them from lysing, and stabilizing hemoglobin levels.

[12] The 810 Patent is the second of three patents owned by Alexion relating to their work on eculizumab. The first patent, Canadian Patent No. 2,189,015 [015 Patent] expired on May 1, 2015. The third patent, Canadian Patent No. 3,022,097 [097 Patent], is also listed on the Patent Register and was initially asserted by Alexion in the present proceedings. However, through amendment to its statements of claim on February 8, 2024, Alexion withdrew its allegations in respect of the 097 Patent and as such, there are no issues for the Court to determine with respect to the 097 Patent.

III. **The 810 Patent**

[13] The 810 Patent is entitled "Treatment of Paroxysmal Nocturnal Hemoglobinuria Patients by an Inhibitor of Complement". It is the national phase entry of a Patent Co-operation Treaty [PCT] application filed on March 15, 2007. The 810 Patent was published on September 20, 2007, issued on December 11, 2018, and will expire on March 15, 2027. While the 810 Patent claims priority to United States [US] Patent Application No. 60/783,070, filed on March 15,

2006, Alexion does not seek to assert this priority date, and all parties agree that March 15, 2007 is the relevant date for assessing anticipation and obviousness.

[14] In the Background of the 810 Patent, the patent discusses PNH and describes it as a hematologic disease that results in intravascular hemolysis. It notes that there have been "no therapies that effectively reduce intravascular hemolysis and improve the associated clinical morbidities in PNH" (810 Patent, Ex1, 1:23-25). The Background identifies eculizumab as a "humanized monoclonal antibody directed against terminal complement protein C5" that has been used in a preliminary clinical study to treat patients with PNH (810 Patent, Ex1, 1:26-30).

[15] In the Summary of the patent, it refers to the phase III study called TRIUMPH, where eculizumab was used to treat patients with PNH and was evaluated for its stabilization of hemoglobin levels (810 Patent, Ex1, 2:1-6). The patent refers to treatment with eculizumab decreasing the amount of lysis and limiting hemoglobin release into the bloodstream, thereby improving the patient's quality of life (810 Patent, Ex1, 2:22-26). The Description of the patent provides additional details on the TRIUMPH study, including patient selection, study design, clinical, safety and pharmacological results, and also refers to a further ongoing phase III safety study called SHEPHERD (810 Patent, Ex1, 40:14-16).

[16] The 810 Patent summarizes various aspects of the invention, including methods for improving the quality of life of a patient with PNH. It explains that in certain aspects of the invention, the application of the patent provides "a pharmaceutical composition comprising an antibody that binds C5 or an active fragment thereof", and that in certain embodiments the

antibody is eculizumab and the pharmaceutical composition is administered to patients having PNH (810 Patent, Ex1, 3:18-23). The patent states that in certain embodiments, the antibody that binds C5 has a heavy chain that consists of SEQ ID NO:2 and a light chain that consists of SEQ ID NO:4 (810 Patent, Ex1, 5:30-33). It provides the full amino acid sequence for SEQ ID NO:2 and SEQ ID NO:4, amongst other sequences (810 Patent, Ex1, 44), which it identifies in the sequence listing as being the sequence for eculizumab.

[17] In the Detailed Description of the 810 Patent, it describes the complement system, including the C3, C3a, C3b, C5 and C5a protein factors. It notes that the beneficial effect of anti-C5 monoclonal antibodies were previously reported in experimental models and clinical trials of other disease conditions (810 Patent, Ex1, 11:18-22).

[18] The 810 Patent refers to suitable anti-C5 antibodies as being known to those skilled in the art and refers to US Patent No. 6,355,245 [US245] (which is related to the 015 Patent through US priority) as teaching an antibody that binds to C5 and inhibits cleavage of C5 into C5a and C5b, thereby decreasing the formation of downstream complement components (810 Patent, Ex1, 14:23-28). The patent states that a “preferred method of inhibiting complement activity is to use a monoclonal antibody which binds to complement C5 and inhibits cleavage” while at the same time allowing the “formation of C3a and C3b which are beneficial to the recipient” (810 Patent, Ex1, 16:19-22). It refers to US245 as disclosing antibodies specific to human complement and states that the antibodies disclosed in US245 include the preferred antibody now named eculizumab (810 Patent, Ex1, 16:23-24).

[19] The 810 Patent includes 16 claims, all of which claim the use of a pharmaceutical composition, except for claims 1 and 2. Before trial, the parties narrowed the claims of the 810 Patent at issue to claims 1 and 2 of the 810 Patent.

IV. **Issues**

[20] The following issues are in dispute:

A. Whether the Asserted Claims are anticipated by United States Patent Application Publication No. 2003/023972 [US972] pursuant to subsection 28.2(1) of the *Patent Act*, RSC 1985, c P-4 [*Patent Act*]?

B. Whether the Asserted Claims would have been obvious to a person skilled in the art [PSA] contrary to section 28.3 of the *Patent Act*?

[21] As required, before engaging in an assessment on anticipation and obviousness, the Court must also necessarily construe the Asserted Claims. Thus, claims construction is also a preliminary issue that must be addressed by the Court.

V. **Witnesses**

[22] Five expert witnesses gave testimony at trial. Three experts were called by Amgen (Dr. Francois Bertelli, Dr. Farid Boulad and Dr. Devendra Kalonia) and two experts were called by Alexion (Dr. Arturo Casadevall and Dr. Peter Tessier). The parties agreed to stipulations as to the expertise of all expert witnesses.

A. *Amgen's Experts*

[23] **Dr. Francis Bertelli:** Dr. Bertelli is the Head of Antibody Research at 272Bio Limited in Reading, United Kingdom (UK), where he leads antibody research, including the discovery of

antibodies for therapeutic use. Since 1998, he has held the position of Principal Scientist and related roles at pharmaceutical companies across the UK, including Pfizer Global Research and Development and Spirogen, a subsidiary of AstraZeneca. He has over 25 years of experience in drug discovery and biotherapeutics development, including oncology, immunology, antibody discovery, engineering, and modelling. He was admitted as an expert in the design and development of humanized monoclonal antibodies, including strategies to reduce immunogenicity and effector functions.

[24] Dr. Bertelli tendered a single expert report opining from the perspective of the antibody engineer on claims construction, anticipation, and obviousness as it related to claim 1 of the 810 Patent.

[25] Overall, I found Dr. Bertelli to be a straight-forward and fair witness whose evidence was of assistance to the Court. However, at times, I found Dr. Bertelli to take a results-oriented approach to the prior art causing me to favour Dr. Tessier's reading of the prior art as set out further below.

[26] **Dr. Farid Boulad:** Dr. Boulad is a physician who obtained his M.D. from the Université de Libre de Bruxelles in Belgium in 1982. Since 2023, he has held the position of Scientific Director at Enfants Cancer Santé, a French fundraising organization for research in pediatric cancer. For over three decades, Dr. Boulad worked as a physician treating pediatric and adult patients with a specialization in hematology oncology and bone marrow failure disorders. From 1991-2022, he held various roles at the Memorial Sloan-Kettering Cancer Center, including

leading the Non-Malignant Hematologic Disorders Centre. He has cared for approximately 20 patients with PNH with various treatments, including SOLIRIS®. Dr. Boulad was admitted as an expert in the human complement system, and the diagnosis, treatment and management of patients suffering from complement-mediated disorders, including PNH.

[27] Dr. Boulad provided a short expert report, addressing the PSA, their common general knowledge [CGK], claims construction, and prior art relevant to the 810 Patent from the perspective of the clinician. He did not opine on anticipation or obviousness or the Asserted Claims.

[28] While I found Dr. Boulad to be a knowledgeable witness, I considered his evidence to be of more limited value as he did not opine on the claims or issues in dispute.

[29] **Dr. Devendra Kalonia:** Dr. Kalonia received his Ph.D. in Pharmaceutics from the University of Connecticut in 1985. Since 2017, he has held the title of Professor Emeritus at the University of Connecticut where, for more than 30 years, he has worked as a researcher and professor. Dr. Kalonia has more than 40 years academic and professional experience in pharmaceutical formulations. His scientific research has focussed on the formulation of peptide and protein pharmaceuticals, with special emphasis on antibody characterization and formulation. Dr. Kalonia was qualified as an expert in the development of stable antibody formulations, including the identification and selection of dosage form, concentration, dose, and excipients.

[30] Dr. Kalonia provided a single expert report, opining as an antibody formulator on claim construction and obviousness of claim 2 of the 810 Patent.

[31] Although I found Dr. Kalonia to be knowledgeable, as my findings on claim 1 were dispositive of claim 2, I do not refer to his evidence in detail in these reasons.

B. *Alexion's Experts*

[32] **Dr. Arturo Casadevall:** Dr. Casadevall is a Professor of Molecular Microbiology, Immunology and Infectious Diseases at the Johns Hopkins Bloomberg School of Public Health. He received his Ph.D. in Biochemistry in 1984 and his M.D. in 1985, both from New York University, and is certified by the American Board of Internal Medicine in Internal Medicine and Infectious Diseases. Dr. Casadevall has over 30 years experience in therapeutic antibody design. For over 15 years, he has researched the effect of antibody constant regions on antibody binding and specificity. He has been directly involved in the development of two monoclonal antibodies for therapeutic treatment and in several clinical trials investigating antibody therapies.
Dr. Casadevall was admitted as an expert in the design, engineering, characterization, development, evaluation, testing (including biological and physiochemical analysis), formulation, and delivery of monoclonal antibodies for use in human clinical therapy.

[33] Dr. Casadevall provided a single expert report, offering opinions on claims construction, anticipation, and obviousness of the Asserted Claims from the perspective of the antibody engineer. He also responded to Dr. Bertelli on these issues.

[34] I have no doubt that Dr. Casadevall is very knowledgeable in his field; however, I found him to be a difficult witness at times, failing to answer questions directly and offering only vague responses. Because of these difficulties I preferred the evidence of Drs. Tessier and Bertelli.

[35] **Dr. Peter Tessier:** Dr. Tessier is a Professor at the University of Michigan in the Departments of Pharmaceutical Sciences, Chemical Engineering and Biomedical Engineering. Since 2007, he has held numerous faculty positions at several American universities. His present research focuses on developing technologies for designing, characterizing, formulating, and delivering therapeutic antibodies, specifically the technological development of engineering and directed evolution of proteins (including antibodies), biomolecular screening and high-throughput characterization of proteins (including antibodies), and machine learning and computational predictions. Dr. Tessier was admitted as an expert in the: (i) design, engineering, and characterization of antibodies, including therapeutic monoclonal antibodies; and (ii) formulation and delivery of therapeutic monoclonal antibodies for use in human clinical therapy.

[36] Dr. Tessier provided three expert reports. His first two reports, which were the same (one for each of T-1094-23 and T-1095-23) addressed the PSA, their CGK and claims construction. His third report opined on the issues of obviousness and anticipation of the Asserted Claims from the perspective of the antibody engineer and the antibody formulator, while also responding to the opinions given by Dr. Bertelli and Dr. Kalonia.

[37] I found Dr. Tessier to be a fair and honest witness, who testified in a careful and considered manner, seeking to assist the Court by providing explanations for his opinions where they were helpful.

C. *Fact Witnesses*

[38] The Plaintiffs introduced one fact witness, Dr. Leonard Bell, who is one of the inventors of the 810 Patent. Dr. Bell is a founder and was the former Chief Executive Officer of Alexion from its inception in 1992 until his retirement in 2015. He also held the position of President and other executive positions at certain times during his tenure. Dr. Bell testified generally as to the work that led to the development of eculizumab (SOLIRIS®) and his involvement in obtaining regulatory approval for the drug in the United States. Dr. Bell was also questioned about certain publications relating to the development work on eculizumab, which were authored by Alexion and included in the prior art, as well as the 015 Patent and US245.

VI. **Claims Construction**

A. *Legal Principles*

[39] The first task for the Court in a patent infringement action is to construe the claims in issue. Claims construction is not a results-oriented exercise. Rather, the claims are to receive one and the same interpretation for all purposes: *Whirlpool Corp v Camco Inc*, 2000 SCC 67 [*Whirlpool*] at para 49(b).

[40] The focus of claims construction is on the language of the claims: *Free World Trust v Électro Santé Inc*, 2000 SCC 66 [*Free World Trust*] at para 39. The specification describes the

invention so that a PSA can understand what the invention is and, when the patent expires, put it into practice, but it is the claims that carve out the boundaries of the proprietary right granted by the patent: *Free World Trust* at para 33; *Merck & Co, Inc v Pharmascience Inc*, 2010 FC 510 at para 44.

[41] Purposive construction involves the Court trying to understand the inventor's objective intention and the particular words or phrases in the claims that describe what the inventor considered to be the essential elements of the invention: *Whirlpool* at para 45; *Free World Trust* at para 31(e); *Biogen Canada Inc v Pharmascience Inc*, 2022 FCA 143 [*Biogen*] at para 74.

[42] Although the claim language must be read through the eyes of a PSA, as equipped with their CGK (*Free World Trust* at paras 44-45; *Tearlab v I-Med*, 2019 FCA 179 at para 32), it is the task of the Court alone to construe the claims as a matter of law (*Biogen* at para 73; *Whirlpool* at para 61). The role of experts is to put the judge in the best position to do so in an informed and knowledgeable way: *Biogen* at para 73; *Whirlpool* at para 57.

[43] I will thus characterize the PSA of the 810 Patent and their CGK before construing the claims of the patents.

B. *The PSA and their CGK*

(1) The PSA

[44] The PSA is a hypothetical person to whom the patent is addressed. They are deemed to be unimaginative and uninventive, but at the same time to have an ordinary level of competence

and knowledge, incidental to the field of the patent, and to be reasonably diligent in keeping up with advances: *AstraZeneca Canada Inc v Apotex Inc*, 2014 FC 638 at para 51, aff'd 2015 FCA 158, rev'd on other grounds 2017 SCC 36. They have a mind willing to understand the specification put before them and are trying to achieve success, rather than look for difficulties or seek failure: *Abbott Laboratories v Canada (Minister of Health)*, 2005 FC 1332 at para 43, aff'd 2007 FCA 153, citing to *Free World Trust* at para 44. This may be a single individual or a team of individuals representing different disciplines, depending on the nature of the invention.

[45] It is the person, or team of individuals, that would work the patent in a real sense: *Takeda Canada Inc v Apotex Inc*, 2024 FC 106 [*Takeda*] at para 76; *Alcon Canada Inc v Cobalt Pharmaceuticals Company*, 2014 FC 462 at para 37, aff'd 2015 FCA 191, 2015 FCA 192.

[46] Where the PSA comprises a team, each person brings their own and collective expertise to the problem. The team is assumed to cooperate such that the deficiency of one addressee may be made up by another: *Westaim v Royal Canadian Mint* (2002), 23 CPR (4th) 9, 2002 FCT 1217 (CanLII) at paras 36-39, citing *Mobil Oil v Hercules* (1994), 57 CPR (3d) 488 at 494, 1994 CanLII 19630 (FC), and Fox, Harold G., *The Canadian Patent Law and Practice Relating to Letters Patent for Inventions*, 4th ed (Toronto: Carswell, 1969) at 185-186.

[47] All experts agreed that the PSA comprises a team that would include an antibody engineer, a formulator with experience formulating antibody compositions, and a clinician with experience treating patients with PNH (Boulad, Ex12, paras 69-70; Bertelli, Ex19, para 89; Kalonia, Ex15, paras 49-50; Casadevall, Ex24, para 41; Tessier, Ex27 and Ex28, para 37;

Tessier, Ex29, para 48). The antibody engineer would have particular interest in claim 1 and the formulator would have particular interest in claim 2.

[48] While the parties were not *ad idem* as to the level of education and experience required of the PSA in each of these disciplines, they ultimately agreed in argument that nothing turned on their differences. In my view, the evidence establishes that each of the members of the skilled team would have a graduate degree (MSc. or Ph.D.), or in the case of a clinician an M.D., coupled with at least several years of experience.

(2) CGK

[49] To properly equip myself for the claims construction exercise, I must also consider the CGK of the PSA. CGK is the knowledge generally known by the PSA at the relevant date; however, it does not include all information in the public domain: *Apotex Inc v Sanofi-Synthelabo Canada Inc*, 2008 SCC 61 [*Sanofi*] at para 37; *Bell Helicopter Textron Canada Limitée v Eurocopter, société par actions simplifiée*, 2013 FCA 219 at paras 64-65. As agreed by the parties, the CGK as of September 2007 (the relevant date for construction) is no different than the CGK as of March 15, 2007 (the date relevant for the invalidity allegations).

[50] The evidence from the experts was consistent that the PSA's CGK at the relevant dates included knowledge of the complement system and the cause and effects of PNH as set out above, as well as the following information:

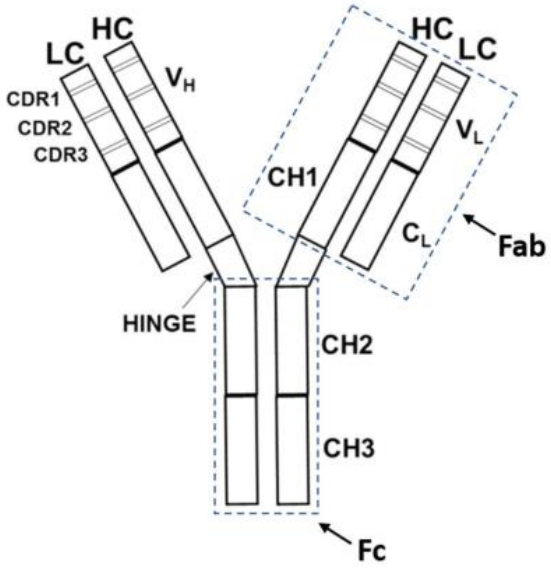
a) Antibodies are complex Y-shaped three-dimensional proteins that have two identical heavy chains (HC) and two identical light chains (LC), each with a

variable region (V_L and $V_{H)}$ at the end of each arm of the Y, and a constant region (C_L and C_H) (Tessier, Ex27 and Ex28, paras 24-25; Casadevall, Ex24, paras 45-46, 50; Bertelli, Ex19, paras 27-29).

b) The sequence of an antibody is important to its three-dimensional structure and its function (Casadevall, Ex24, paras 48, 388; Bertelli CX, TT 473:20-474:8; Tessier, Ex29, para 57).

c) The sequence of the antibody's constant region depends on the class of the antibody. The most common antibody class in humans is IgG (Tessier, Ex29, para 53; Casadevall, Ex24, paras 48-49; Bertelli, Ex19, para 30).

d) The variable region of IgG consists of three complementarity-determining regions (CDR1, CDR2, CDR3) and framework regions surrounding the CDRs. The constant region of each of the heavy chains of IgG is comprised of three domains CH1, CH2 and CH3 with a hinge region connecting the arms of the Y to the base. The CH2 and CH3 regions of the heavy chains are called the fragment crystallizable (Fc) region; while the light chain, and the variable region and CH1 domain of the heavy chain are together called the fragment antigen-binding (Fab) region (Bertelli, Ex19, paras 33-36; Tessier, Ex27 and Ex28, paras 25-26; Casadevall, Ex24, paras 47, 50-51). The basic structure of an IgG antibody is depicted in the figure below from Dr. Casadevall's expert report (Ex24, para 49), a version of which also appears in the expert reports of Drs. Tessier (Ex27 and Ex28, para 27) and Bertelli (Ex19, para 29):



e) It is the variable regions of antibodies that contain antigen binding sites. Antigen specificity is characterized by the CDRs, with CDR3 often being the most important for binding (Tessier, Ex27 and Ex28, para 25; Tessier CX, TT 1027:9-13, 1048:20-23; Bertelli, Ex19, para 33; Bertelli DX, TT 399:7-16; Casadevall, Ex24, para 47; Casadevall CX, TT 673:18-674:3, 676:1-10).

f) The Fc region of the antibody's constant region mediates effector functions, such as activating complement and interacting with Fc receptors that are expressed on a range of cell types (Tessier, Ex29, para 54; Bertelli, Ex19, para 35; Casadevall, Ex24, para 51; Bertelli DX, TT 396:7-20).

g) Within the IgG class of antibody there are four subclasses (IgG1, IgG2, IgG3 and IgG4) which have different binding specificity due to their amino acid sequences (Tessier, Ex29, para 53; Bertelli, Ex19, para 38; Casadevall, Ex24, paras 60, 171), and different abilities to elicit effector functions. The IgG4 subclass has no complement activity, while both the IgG2 and IgG4 subclasses have diminished

effector function activity relative to the IgG1 and IgG3 subtypes (Bertelli, Ex19, paras 38-42; Bertelli DX, TT 397:22-398:19; King 1998, Ex29, FC236, at 8 (Table 1.1); Bertelli CX, TT 472:3-473:19; Casadevall, Ex24, para 60; Tessier CX, TT 938:7-16).

h) Computer databases existed which contained the amino acid sequences of known proteins, including native antibodies and their constant regions (Bertelli, Ex19, para 76; Bertelli DX, 395:11-17; Bertelli CX, TT 593:4-23; Casadevall CX, TT 797:23-798:13; Tessier, Ex29, para 205). A researcher could access such databases to determine whether an unknown sequence had any sequence homologies to a known sequence in the database (Bertelli, Ex19, para 76; Casadevall CX, TT 698:5-14, 798:4-13; Tessier, Ex29, para 205).

i) Laboratory techniques existed to produce, isolate, and characterize monoclonal antibodies (typically in mice) for a particular antigen that had a single unique amino acid sequence for its variable and constant regions (Casadevall, Ex24, paras 53-54, 167; Tessier, Ex29, para 55; Bertelli, Ex19, paras 46-48).

j) Monoclonal antibodies for human therapeutic use (*i.e.*, chimeric antibodies, humanized antibodies) could be designed or engineered from sequences derived from human and animal antibodies using known cloning techniques. Chimeric antibodies combine the variable regions of an animal antibody with human constant regions, while humanized antibodies combine the CDRs of animal into the human variable antibody structure (Tessier, Ex29, paras 56-57; Casadevall,

Ex24, paras 54, 169; Bertelli, Ex19, paras 45-47, 56; Bertelli DX, TT 401:6-402:1).

k) Antibody fragments such as Fab fragments and single chain variable fragments (scFv) could function as stand-alone constructs that could be used as research tools and as therapeutics (Tessier, Ex29, para 60; Casadevall, Ex24, paras 56-57; Bertelli, Ex19, para 36).

l) Monoclonal antibodies cannot be directly administered to patients but must be administered as a formulation or pharmaceutical composition, typically in aqueous or lyophilized (freeze-dried) form. Pharmaceutical compositions of an antibody would include a combination of the monoclonal antibody and other inactive ingredients, often called excipients (Tessier, Ex29, paras 242-243; Tessier DX, TT 956:9-957:4; Kalonia, Ex15, paras 28-30, 33; Kalonia DX, TT 266:15-21).

m) An antibody formulation must have both chemical and physical stability to be used as a pharmaceutical composition. Several antibody formulations existed and were approved as drugs in Canada and the United States at the relevant dates (Kalonia, Ex15, paras 27, 29; Kalonia DX, TT 267:1-268:2, CX, TT 302:18-303:8; Casadevall DX, TT 621:22-622:5; 810 Patent, Ex1, 22:21-25, 24:7-9, 17-19).

n) Alexion had a drug, named eculizumab, targeting C5 that it was using in preliminary clinical studies to treat patients with PNH that had shown promising

results (Boulad, Ex12, paras 47-53, 264; Bertelli, Ex19, paras 93-94; Casadevall CX, TT 743:7-16; see also TT, 1225:11-13 where the parties agree that Hillmen 2004 (defined below) was CGK).

C. *Construction of the Asserted Claims*

[51] The 810 Patent includes 16 claims, only two of which are at issue in this proceeding (claims 1 and 2).

[52] Claims 1 and 2 of the 810 Patent read as follows:

> 1. An antibody that binds C5 comprising a heavy chain consisting of SEQ ID NO:2 and a light chain consisting of SEQ ID NO:4.
>
> 2. A pharmaceutical composition comprising the antibody of claim 1 and a carrier.

[53] Claim 1 claims a full-length antibody that binds C5 and has the heavy chain amino acid sequence of SEQ ID NO:2 and the light chain amino acid sequence of SEQ ID NO:4. SEQ ID NO:2 and SEQ ID NO:4 are identified in the 810 Patent as the respective heavy and light chain sequences for eculizumab and are defined as follows:

SEQ ID NO: 2 – Eculizumab Heavy chain

QVQLVQSGAEVKKPGASVKVSCKASGYIFSNYWIQWVRQAPGQGLEWMGEILPG
SGSTEYTENFKDRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARYFFGSSPNWYF
DVWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNS
GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVE
RKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFN
WYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP
SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQ
PENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSL
SLSLGK

SEQ ID NO: 4 – Eculizumab Light chain

DIQMTQSPSSLSASVGDRVTITCGASENIYGAL
NWYQQKPGKAPKLLIYGATNLADGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQ
NVLNTPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKV
QWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQG
LSSPVTKSFNRGEC

[54] There is no real dispute that all elements of claim 1 are essential to the invention as claimed. While Amgen argues that it was not necessary for Alexion to claim the antibody's ability to bind C5 as this ability is an inherent property of an antibody with the sequence claimed, this is more an argument of redundance than one of essentiality. Indeed, Amgen's own expert, Dr. Bertelli, referred to the essentiality of all elements of claim 1 (Bertelli, Ex19, para 96).

[55] The sole disagreement between the experts on claim construction is whether the PSA would understand "binds C5" to mean selective binding of C5 complement protein and no other complement factors, including C3, as this is not specified in the claim. As explained by Dr. Casadevall, the PSA would understand based on their CGK that antibody specificity was important if the antibody was to be considered as a therapeutic agent in humans (Casadevall, Ex24, para 85). Indeed, the 810 Patent states that: "[s]pecific antibodies capable of inhibiting complement, such as an antibody that binds C5, are relatively specific and do not block the functions of early complement component. In particular, such specific agents will not substantially impair the opsonization functions associated with complement component C3b, which functions provide a means for clearance of foreign particles and substances from the body." (810 Patent, Ex1, 15:22-26; Tessier, Ex29, para 73). In my view, on a purposive construction of claim 1, the PSA would understand that the antibody claimed binds C5 with this type of selectively.

[56] With respect to claim 2, the experts generally agreed that the term "pharmaceutical composition" refers to the claimed antibody in combination with a "carrier", which together are intended to be administered for therapeutic use (Kalonia, Ex15, para 54; Tessier, Ex29, para 75; Casadevall, Ex24, para 90). The experts agreed that the "carrier" refers to the non-medicinal ingredients in the pharmaceutical composition that allow the pharmaceutical composition to be delivered to the patient. In the context of an antibody composition, the experts agreed that the "carrier" would allow the antibody to be administered to the patient as a solution (Kalonia, Ex15, para 57; Kalonia DX, TT 273:3-11; Casadevall, Ex 24, para 91; Tessier, Ex29, para 75; Tessier CX, TT 956:9-22; 810 Patent, Ex1, 2:22-25).

VII. **Anticipation**

[57] The proposed invention claimed in a patent must be new to be patentable. Subsection 28.2 of the *Patent Act* sets out the requirement for novelty of a patented invention. As relevant to this proceeding, paragraphs 28.2(1)(a) and (b) read as follows:

28.2 (1) The subject-matter defined by a claim in an application for a patent in Canada (the "pending application") must not have been disclosed	**28.2 (1)** L'objet que définit la revendication d'une demande de brevet ne doit pas:
(a) before the one-year period immediately preceding the filing date or, if the claim date is before that period, before the claim date by the applicant, or by a person who obtained knowledge, directly or indirectly, from the applicant, in such a manner that the subject-	**a)** soit plus d'un an avant la date de dépôt de celle-ci, soit, si la date de la revendication est antérieure au début de cet an, avant la date de la revendication, avoir fait, de la part du demandeur ou d'un tiers ayant obtenu de lui l'information à cet égard de façon directe ou

matter became available to the public in Canada or elsewhere;	autrement, l'objet d'une communication qui l'a rendu accessible au public au Canada ou ailleurs;
(b) before the claim date by a person not mentioned in paragraph (a) in such a manner that the subject-matter became available to the public in Canada or elsewhere;	**b)** avant la date de la revendication, avoir fait, de la part d'une autre personne, l'objet d'une communication qui l'a rendu accessible au public au Canada ou ailleurs;

[58] Amgen asserts that claims 1 and 2 of the 810 Patent are anticipated by US972, which is a patent application published on December 18, 2003, that identifies API in its address for correspondence and Katherine Bowdish, an Alexion employee, as one of its inventors.

[59] The parties agree that US972 is citable prior art under both paragraph 28.2(1)(a) and paragraph 28.2(1)(b) of the *Patent Act* as its publication date satisfies each of these provisions.

[60] The SCC in *Sanofi* set out two requirements for establishing anticipation: prior disclosure and enablement. To meet the requirement for prior disclosure, there must be clear direction so that a PSA would in every case and without possibility of error be led to the claimed invention; a signpost will not suffice: *Free World Trust* at para 26; *Western Oilfield Equipment Rentals Ltd v M-I LLC*, 2021 FCA 24 [*Western Oilfield*] at para 82. While it is not necessary that "the exact invention" be publicly disclosed, the prior disclosure must be of subject matter which, if performed, would necessarily result in infringement of that patent: *Sanofi* at paras 23, 25. To meet the requirement for enablement, the PSA must have been able to perform the invention at the relevant date: *Sanofi* at para 26. At this stage of the analysis, the question is not about what the PSA would think the disclosure of the prior reference meant, but whether the PSA using the

prior reference would be able to work the invention using only trial and error experimentation: *Sanofi* at para 27.

[61] While both prior disclosure and enablement are disputed, the focus of the debate between the parties is on whether there was prior disclosure of the invention as claimed. To meet this requirement "there is no room for trial and error or experimentation by the skilled person. He is simply reading the prior patent for the purposes of understanding it": *Sanofi* at para 25. If there is any doubt about what a prior art reference discloses, it cannot be taken to meet the definition of anticipation: *Gilead v Canada*, 2013 FC 1270 at para 30; *Bristol-Myers Squibb Canada Co v Teva Canada Limited*, 2016 FC 580 [*BMS*] at para 243; aff'd 2017 FCA 76; *Sanofi* at para 21, citing *General Tire & Rubber Co v Firestone Tyre & Rubber Co*, [1972] RPC 457 at 486; *Takeda* at para 152; *Boehringer Ingelheim v JAMP*, 2024 FC 1198 at para 152.

[62] As noted in *Takeda* at paragraph 153, disclosure may be made without any recognition of what is present or what is happening: see *Abbott Laboratories v Canada (Minister of Health)*, 2008 FC 1359 at para 75 [*Abbott*]; aff'd 2009 FCA 94. If in performing the teachings of the prior art reference, the invention is necessarily made, the absence of knowledge of the subject-matter of the invention is legally irrelevant: *Abbott v Canada (Minister of Health)*, 2007 FCA 153 at paras 18-22. However, if there are choices left for the PSA, leading to other ways to perform the prior art which do not result in infringement, there will be no anticipation: *BMS* at para 232; *Apotex v Shire*, 2021 FCA 52 [*Shire*] at para 50.

[63] US972 is entitled “Rationally Designed Antibodies” and relates generally to the use of antibodies or antibody fragments as a framework for mimetic peptides to provide the peptides with enhanced stability (Tessier, Ex29, para 112; Bertelli, Ex19, paras 119-121).

[64] In Example 4 of US972, a mimetic peptide (*i.e.*, the hormone, thrombopoietin (TPO)) is transplanted into the heavy chain CDR3 of the antibody framework “5G1.1” (Tessier, Ex29, para 113; Casadevall, Ex24, para 116; Bertelli, Ex19, para 121).

[65] In his expert report and during testimony, Dr. Bertelli focussed his anticipation analysis on the first paragraph (paragraph [0191]) of Example 4 of US972, which reads as follows:

Example 4

[0191] The TPO mimetic peptide graft in Fab clone X4b has been transplanted into the heavy chain CDR3 of another antibody framework, 5G1.1. Construction of 5G1.1 is described in U.S. Application. Ser. No. 08/487,283, incorporated herein by reference. The sequence was cloned into 5G1.1 in such a fashion as to replace the native CDR3 with 5' ttg cca ATT GAA GGG CCG ACG CTG CGG CAA TGG CTG GCG GCG CGC GCG cct gtt 3' (SEQ. ID. NO: 65). The peptide graft translated into amino acids is Leu Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Pro Val (SEQ. ID. NO: 66). The 5G1+peptide was produced as a whole IgG antibody (See **FIGS. 13A and 13B**).

[66] Paragraph [0191] discloses the preparation of an antibody (5G1[.1] + peptide) with a TPO mimetic peptide transplanted in place of the native CDR3 of the heavy chain of the 5G1.1 scaffold. The sequence of the 5G1[.1] + peptide, which was produced as a whole IgG antibody, is set out in FIGS 13A and 13B of US972 and has the heavy chain amino acid sequence of SEQ

ID NO:67 and the light chain amino acid sequence of SEQ ID NO:69. US972 does not provide the sequence of the CDR3 or of the original 5G1.1 framework.

[67] It is undisputed that SEQ ID NO:69 discloses the same sequence as the light chain of eculizumab (SEQ ID NO:4 of the 810 Patent) (Bertelli, Ex19, para 146; Bertelli DX, TT 417:11-15; Tessier, Ex29, para 190, Casadevall CX, TT 694:21-695:1) and that SEQ ID NO:67 discloses a heavy chain sequence that is the same as the heavy chain sequence of eculizumab (SEQ ID NO:2 of the 810 Patent), but for the inclusion of the TPO mimetic peptide instead of the CDR3 of the heavy chain (Bertelli, Ex19, para 143; Tessier, Ex29, para 190; Casadevall CX, TT 692:1-8).

[68] The experts agree that the 5G1[.1] + peptide that is disclosed in Figures 13A and 13B is a humanized antibody (Tessier CX, TT 1021:7-14, 1023:12-19, 1025:20-24; Bertelli, Ex19, para 126; Bertelli DX, TT 421:13-422:9; Casadevall CX, 696:4-12, 700:13-16). Amgen asserts that it can therefore be inferred that the originating 5G1.1 antibody framework was humanized. As such, it argues that the PSA can simply look to US245 (which the parties agree has the same content as its originating application, US Application Serial No. 08/487,283) for its humanized constructs to find the sequence of the heavy chain CDR3, which if transplanted back into the 5G1[.1] + peptide would give the PSA the sequence of eculizumab.

[69] As a preliminary matter, Alexion takes issue with Amgen's reliance on US245 as part of the teaching of US972. It asserts that anticipation will only be established if a single prior art document gives the PSA all the information needed to produce the claimed invention without the

exercise of inventive skill. As US972 does not itself disclose the full sequence of eculizumab (a point which Amgen does not dispute), Alexion argues it cannot anticipate the Asserted Claims of the 810 Patent.

[70] Alexion further contends that even if US245 is considered along with US972, any reliance on US245 is limited to its teaching regarding the source of the initial 5G1.1 framework antibody, which is not eculizumab. Alexion contends that US972 does not teach the construction of eculizumab from the 5G1[.1] + peptide, nor is eculizumab necessarily made in the preparation of the 5G1[.1] + peptide antibody.

A. *Incorporation by Reference*

[71] As noted by Amgen, the language of the relevant provision of the *Patent Act* dealing with anticipation has changed over time. Prior to October 1989, subsection 27(1) of the *Patent Act* referred to anticipation by a prior patent or printed publication and not anticipation by prior disclosure, which is the language of the *Patent Ac*t's current section 28.2: see *Abbott* at para 59. Amgen asserts that this is a meaningful change intended to focus the anticipation analysis on a single prior disclosure, instead of limiting the analysis to a single patent document.

[72] Alexion disagrees that there is a distinction, and cautions against conflating anticipation with obviousness, referring to the warning provided by Justice Phelan in *Hospira Healthcare Corporation v Kennedy Trust for Rheumatology Research*, 2021 FC 42 [*Hospira*] at paragraph 57 against combining references for anticipation:

> [57] Moreover, Pfizer's position on anticipatory disclosure requires that one piece of prior art (*'94 Kennedy*) should be read in

> conjunction with a second piece of prior art (*Elliott*) which is cited in the first. This is an erroneous approach to anticipation as it conflates anticipation and obviousness.

[73] In providing his comments, Justice Phelan refers to *Free World Trust*, which cites to foundational statements made by Justice Hugessen in *Beloit Canada Ltd v Valmet OY* (1986), 8 CPR (3d) 289, 64 NR 287 (FCA) [*Beloit*]:

> [58] With respect to anticipation, *Free World Trust* adopted the classic statement from *Beloit* at para 29:
>
> > One must, in effect, be able to look at a single publication and find in it all information, which, for practical purposes, is needed to produce the claimed invention without the exercise of inventive skill. The prior publication must contain so clear a direction that a skilled person reading and following it would in every case and without possibility of error be led to the claimed invention.
> >
> > (Emphasis added)
>
> [59] Given *Beloit's* reference to a single publication, the approach to refer to a second or more publications violates this teaching. Taken to its logical limits, mosaicking multiple other publication references within a single piece of art could be anticipatory.

[74] Amgen contends that a distinction must be made between prior art documents referring to other documents in footnotes as supporting references and those that seek to make clear to the PSA that a reference is being incorporated to complete the disclosure. It notes that in *Hospira* there is no suggestion that the reference made within the prior art document was an incorporation by reference relating to the disclosure, as in the present case.

[75] Amgen refers to the cross-examination of Dr. Tessier where, when asked about references to other documents that were made in his own authored US patents, he acknowledged

the distinction between general references and those intended to convey specific information important for understanding the disclosure in the patent (Tessier CX, TT 987:15-988:22, 990:24-992:10).

[76] As asserted by Amgen, incorporation by reference is a common patent drafting practice in the United States (Evan Bender *et al*, "The Ins and Outs of Incorporation by Reference" (2023) 35:10 IP & Tech LJ 1 at 2) and is one of the limited exceptions contemplated by the Canadian *Manual of Patent Office Practice* [MOPOP] where a prior disclosure could comprise teachings from more than a single document. According to the MOPOP section 18.01.05, this may occur where "a primary source of information makes explicit reference to specific teachings in a secondary source, thereby making clear to the skilled reader that the teachings of the secondary source are to be relied on in order to understand or complete the disclosure of the invention in the primary source."

[77] Although this statement from the MOPOP is not binding, it is nonetheless helpful and, in my view, is consistent with the principles outlined in *Free World Trust* and *Beloit*.

[78] The critical factor is whether the prior reference provides clear direction so that the PSA arrives inevitably at the claimed invention. Where an incorporation by reference is used, this will depend on what directions are provided in the primary source as to how the incorporated reference is to be used.

[79] As the MOPOP extract proposes, clear direction may be provided where the primary source "makes explicit reference to specific teachings in a secondary source" thereby giving the PSA precise direction to the specific information that is to be included in the disclosure. In such instance, in my view, the incorporated reference is not being used to add new teachings to the primary document to create a cumulative effect where the PSA is left to look to multiple sources to determine what information to combine. Rather, the primary source leads the PSA directly to the information that completes the disclosure.

[80] Thus, in my view, the sole fact that Example 4 of US972 uses an incorporation by reference is not enough, on its own, to conclude on anticipation. The critical question is what is disclosed to the PSA by reading Example 4 of US972 and the reference in paragraph [0191] to US Application Serial No. 08/487,283 (hereinafter referred to as US245).

B. *Is the incorporation by reference to US245 a single disclosure with US972?*

[81] As a starting point, it bears repeating that a prior art document is to be given the same type of purposive interpretation as the patent at issue, with its teachings read as a PSA would have understood them: *Shire Biochem Inc v Canada (Health)*, 2008 FC 538 at para 65; *Whirlpool* at para 49(c); *Eli Lilly Canada Inc v Apotex Inc*, 2007 FC 455 at para 252, aff'd 2008 FCA 44.

[82] As set out earlier, US972 is a patent relating to the use of antibodies or antibody fragments as a framework for stabilizing mimetic peptides. Example 4 uses "5G1.1" as the antibody framework for production of the recombinant "5G1[.1] + peptide" antibody product. Paragraph [0191] states that "[c]onstruction of 5G1.1" is described in US245, which it

incorporates by reference, but it does not direct the PSA to any particular paragraph in US245 as guidance. US245 discloses the murine monoclonal antibody "5G1.1" (and its preparation) and 26 other anti-C5 antibody fragments and molecules prepared from 5G1.1, including humanized fragments (Ex7, FC51, examples 7 and 11; Tessier DX, TT:903:4-18; Casadevall, Ex24, para 127).

[83] According to Dr. Tessier, the PSA would have understood "5G1.1" as used in the first sentence of paragraph [0191] (shown in paragraph [65] above) to be referring to the murine antibody described in US245 (not eculizumab) and from the context of the second sentence, that US245 was being referenced only for the limited purpose of disclosing the source of the hybridoma that produced 5G1.1 (Tessier CX, TT 921:16-20; Tessier, Ex29, para 195). They would not have understood that the entirety of US245 was being incorporated into US972, particularly as US245 was only referenced in connection with the "construction of 5G1.1" and did not refer to US245 being incorporated in its entirety as US972 had done with other documents (Tessier, Ex29, paras 194, 216).

[84] Dr. Bertelli acknowledged that US245 used the "5G1.1" nomenclature to refer to the murine antibody and disclosed the details of the hybridoma that made the murine 5G1.1 antibody and its deposit with the American Type Culture Collection (Bertelli CX, TT 525:5-526:18; 584:12-15). However, because the final 5G1[.1] + peptide referenced in paragraph [0191] of US972 was a humanized antibody, he opined that to make the 5G1[.1]+ peptide, the PSA would start with a humanized framework and that the reference to 5G1.1 in the first sentence of

paragraph [0191] of US972 must therefore be referring to a humanized antibody framework (Bertelli, Ex19, para 140; Bertelli DX, TT 423:22-424:8).

[85] While acknowledging that US245 did not disclose any full-length humanized antibodies (Bertelli CX, TT 526:25-527:7, 581:25-582:2, 588:9-12), Dr. Bertelli set out to look for the amino acid sequence of the CDR3 of the heavy chain to then work backwards from SEQ ID NO: 67 to obtain the full-length sequence for the humanized 5G1.1 heavy chain (Bertelli DX, TT 430:16-431:1). He opined that the reference to US245 in US972 was directing the PSA to the CDR3 sequence from US245 and that the PSA would have been directed specifically to the humanized fragments in US245 as US972 pertained to antibodies for human therapeutic use (Bertelli, Ex19, paras 130, 136, 138-140; Bertelli DX, TT 424:4-15).

[86] The exercise proposed by Dr. Bertelli thus involves using reverse engineering to obtain a 5G1.1 antibody that Dr. Bertelli infers is the original 5G1.1 construct. It focusses on using US245 to identify the CDR3 that was removed from 5G1.1, instead of using US245 to identify the 5G1.1 antibody framework. In my view, this approach extends beyond the teachings and disclosure made by US972.

[87] First, as highlighted by Dr. Tessier, US972 does not direct the PSA to use the 5G1[.1] + peptide that is made by Example 4 as a scaffold to recreate 5G1.1 antibodies (Tessier, Ex29, para 194; see also Casadevall, Ex24, para 137). US972 does not discuss any type of reverse cloning exercise. Nor does it instruct the PSA to go to US245 for this purpose (Tessier, Ex29, para 215; Tessier DX, TT 921:21-24).

[88] Second, as US245 discloses only humanized fragments, not full-length humanized antibodies, the exercise proposed by Dr. Bertelli contemplates construction of a 5G1.1 antibody that was not specifically disclosed or made in US245, or one that is different than the original construct (*i.e.*, an antibody framework that is a whole antibody and not one where the constant regions are added after TPO peptide transplantation to produce a "whole IgG antibody" as specified in the last sentence of paragraph [0191] of Example 4).

[89] Moreover, the approach taken by Dr. Bertelli is akin to using the incorporation by reference to mosaic information from US245 with teachings from US972. Rather than being directed by US972 to specific information in US245 to provide the details of the 5G1.1 originating antibody framework, Dr. Bertelli proposes using US245 to search through, find and compare all of the various humanized fragments with heavy chain sequences (12 in total) in order to identify the missing CDR3 sequence that the PSA could then use to make a humanized antibody with the heavy chain sequence of eculizumab (Bertelli, Ex19, paras 140, 142; Bertelli DX, TT 422:25-424:15). He also discusses a confirmation step where the PSA would need to compare SEQ ID NO:67 and SEQ ID NO:69 from US972 with the variable region sequences provided in US245 to identify sequence alignments (Bertelli, Ex19, para 141).

[90] While Dr. Bertelli asserts that each of these steps was straight-forward and would have taken the PSA only a modest amount of time to complete, they necessitate the PSA choosing specific bits and pieces from US245 and assembling this with other information from US972. This amounts to more than mere direction from US972 to specific information in US245.

[91] In my view, Amgen's reliance on US245 is not consistent with it being a single disclosure with US972. While this finding is sufficient to conclude that US972 does not meet the disclosure requirement for anticipation, I will nonetheless go on to consider whether a more expansive incorporation by reference of US245 would result in disclosure of all elements of the Asserted Claims of the 810 Patent and in particular SEQ ID NO:2.

C. *Does US972 anticipate the Asserted Claims with US245 incorporated fully by reference?*

[92] Even if I were to accept that US245 could be used in the manner proposed by Amgen and incorporated by reference more broadly, I am nonetheless of the view that US972 does not anticipate claims 1 and 2 of the 810 Patent. I do not agree that following Example 4 would necessarily lead to the preparation of eculizumab or that the PSA would inevitably conclude that eculizumab is the originating 5G1.1 antibody framework for Example 4.

[93] As stated earlier, for there to be anticipation, the prior art reference must necessarily lead to the claimed invention. If there is any ambiguity or if there are multiple ways that a PSA could interpret the prior art reference and perform its teachings, not all of which lead to the claimed invention, then anticipation will not be found.

[94] In this case, I do not agree that the evidence establishes that the PSA would inevitably be led to eculizumab (and its sequence) by following Example 4 of US972.

[95] While Dr. Tessier acknowledged that a possible approach to make the product of Example 4 could include starting with humanized 5G1.1 that had a IgG2/IgG4 hybrid constant

region, he was steadfast that this approach would only arise as a matter of hindsight and that the PSA would not have read paragraph [0191] in this manner (Tessier CX, TT 1027:17-1028:3, 1030:21-1031:4).

[96] Rather, Dr. Tessier testified that a more reasonable reading of paragraph [0191] instructs the PSA to start with the murine 5G1.1 antibody as this accords with the language in the example and the 5G1.1 terminology used in US245, which refers to 5G1.1 as a native murine antibody (Tessier CX, 1019:6-25, 1023:20-1024:9, see also Casadevall DX, 646:24-647:12, CX, TT 704:19-22; Bertelli CX, TT 584:12-15). The murine 5G1.1 antibody was the only full-length antibody specifically disclosed in US245, as conceded by all experts (Bertelli CX, 526:25-527:7, 581:25-582:2, 588:9-12; Casadevall, Ex24, paras 127, 232; Tessier, Ex29, paras 161, 173).

[97] The PSA would transplant the TPO mimetic peptide in place of the CDR3 on the heavy chain of the murine 5G1.1 antibody framework, test to confirm that the resulting peptide construct bound to its target receptor, humanize the variable region, and then add the human IgG2/IgG4 constant region (Tessier CX, TT 1019:12-25, 1030:3-8, 1043:5-19, Tessier, Ex29, para 173). This same view of starting and transplanting into the murine antibody was also expressed by Dr. Casadevall (Casadevall CX, TT 698:24-699:13, 700:17-23).

[98] Amgen asserts that starting with a murine antibody is not consistent with the broader teachings and uses contemplated by US972. It points to the description of US972, which teaches a preference for using a human antibody or humanized fragment as a scaffold sequence to allow

for the ultimate construct to be used as a human therapeutic (US972, Ex19, FC281, paras 19, 66; Bertelli, Ex19, para 140):

> [0019] Any immunoglobulin molecule (antibody) or fragment thereof could potentially provide the framework and have a CDR replaced with a peptide according to the present disclosure. For therapeutic or in vivo diagnostic use it is preferable that the antibody is of human origin or humanized, ….
>
> […]
>
> [0066] Any antibody can serve as a scaffold sequence, however typically human antibodies are chosen as human therapeutics is one of the ultimate objectives. Human or humanized antibodies are less likely to cause an adverse immune response in a human patient.

[99] However, I accept the explanation of Dr. Tessier that a humanized antibody product would nonetheless meet the objectives for use as a human therapeutic even if it were made from a starting antibody framework that was not human, but was only later humanized (Tessier CX, TT 1030:9-20).

[100] Further, even with a humanized scaffold, it would also be consistent with paragraph [0191] and the above passages for the PSA to make the 5G1[.1] + peptide from a humanized 5G1.1 fragment constructed from the murine 5G1.1 antibody (as was done in US245), transplant the TPO mimetic peptide in place of the CDR3 on the heavy chain, and then add the IgG2/IgG4 hybrid human constant regions to make the full antibody. Indeed, Dr. Bertelli acknowledged that the PSA would start with a humanized fragment as a framework instead of a full-length humanized antibody and that transplantation of the CDR3 for the mimetic peptide occurred within this fragment (Bertelli CX, TT 583:18-584:11, 587:20-588:12)

[101] This interpretation is also consistent with US245, which proposes only generally, as a secondary step, that "matched pairs of the variable regions (e.g., a VL and a VH region) of the various antibody molecules, Fds, and light chains" described in US245 could be combined with IgG constant region domains which may be unaltered, or constructed of a mixture of constant domains of different IgG subtypes, using recombinant DNA or other methods known in the art to form full length antibodies (Ex7, FC51, col 45:24-33). Although, no full-length antibodies were specifically disclosed or constructed.

[102] In this scenario, along with the earlier one described by Dr. Tessier, eculizumab would not be produced in arriving at the 5G1[.1] + peptide as the constant region domains would not be added until after peptide transplantation.

[103] Amgen argues that these options are not supported by paragraphs [0192] and [0193] of US972 (reproduced below), which outline experiments for testing the binding of the peptide in the 5G1.1 + peptide antibody to its receptor. It asserts that the parental 5G1.1 negative control referenced in these experiments, which is described as "parental 5G1.1 without the TPO mimetic peptide" in paragraph [0192] and "parental 5G1.1 not containing the peptide" in paragraph [0193], confirms that the starting 5G1.1 antibody scaffold referenced in paragraph [0191] is a humanized full-length antibody (*i.e.*, eculizumab):

[**0192**] Purified 5G1.1+peptide antibody as well as the parental 5G1.1 were analyzed for their ability to bind to cMpl receptor by FACS analysis. Binding to receptor expressing and non-receptor expressing 293 cells was compared. See **FIG. 14**. The FACS staining was performed essentially as described previously herein, with the exception that the detection was done using PE conjugated F(ab')2 fragment of goat anti-human IgG (H+L). The negative controls of 3° only anti-tetanus toxoid irrelevant Fab, and Fab X1a which binds weakly to cMpl receptor all showed very little staining. However, binding Fabs X1c and X4b showed strong staining as did the 5G1.1+peptide. None of those clones demonstrated binding to the non-receptor expressing cells indicating that the cell staining is occurring through specific recognition of the cMpl receptor. The parental 5G1.1 without the TPO mimetic peptide did not show staining to any of the cells tested.

[**0193**] The ability of the 5G1.1 +peptide whole IgG to activate the cMpl receptor using the luciferase reporter assay has been determined (see **FIG. 15**). The results herein indicate that the configuration of a whole IgG causes steric limitations in its ability to productively bring the two cMpl receptors together for activation. The activity of the 5G1.1 full IgG construct containing the TPO mimetic peptide in the heavy chain CDR3 positions, was only weakly activating and required approximately 100-200 fold higher molar concentrations as compared to TPO, to stimulate equivalent activity. As was previously observed with the binding experiments, activation by the 5G1.1 containing the peptide was observed only when the cMpl-R was expressed on the cell surface. No receptor specific binding or activity was observed with the parental 5G1.1 not containing the peptide. These results demonstrate that binding and activity of the TPO mimetic peptide and selected amino acid flanking sequences is not limited to or specific for the Tetanus Toxoid antibody framework, but can be applied to other antibody frameworks. Thus the flanking amino acid sequences that were selected during panning are specific for presentation of the TPO mimetic peptide within a given CDR position, but not for amino acid sequence of the antibody framework.

[104] However, I have trouble with this argument for two reasons.

[105] First, there is no direct evidence before me as to how paragraphs [0192] and [0193] would be interpreted. Indeed, paragraphs [0192] and [0193] were not considered by Dr. Bertelli in his expert report or in his testimony, nor were these paragraphs highlighted in support of his opinion. Admittedly, paragraph [0192] was only raised for the first time in cross-examination of Alexion's experts, while paragraph [0193] was not raised at all with any of the experts. Even then, neither Dr. Tessier nor Dr. Casadevall provided evidence to support the proposition advanced by Amgen.

[106] According to Dr. Tessier, while the "so-called best [negative] control" for the assay described in paragraph [0192] would be an antibody where the only difference between the parental 5G1.1 negative control and the test antibody (5G1.1 + peptide) was the presence of the TPO peptide in the test antibody, the most important part of the control was to avoid non-specific binding of the secondary reagent, which in the assay was goat anti-human IgG. This would require the antibodies to have complementary constant regions (Tessier CX, TT 1033:15-1034:14). He concluded accordingly that the parental 5G1.1 control used for the assay of paragraph [0192] was most likely not a humanized antibody, but rather a chimeric antibody containing murine variable regions and human IgG2/IgG4 constant regions (Tessier CX, TT 1035:4-1036:6).

[107] Like Dr. Tessier, Dr. Casadevall acknowledged that the best negative control would be an antibody in which the only difference would be the TPO peptide in the test antibody (Casadevall

CX, TT 709: 11-16). However, Dr. Casadevall did not agree that using a goat antihuman IgG secondary reagent meant that the reagent would only bind to human IgG. Instead, he noted that antibodies sometimes react across species. As such, he did not agree that paragraph [0192] established that the parental 5G1.1 control for the assay must be a human antibody (Casadevall CX, TT 715:10-716:9).

[108] While Amgen raises some criticism of this evidence, without any direct evidence to the contrary, this is insufficient for me to adopt the inference that Amgen urges. This is particularly so as the requested inference is also inconsistent with Dr. Bertelli's earlier cited evidence relating to paragraph [0191] in which he opined on transplantation of the TPO peptide into a 5G1.1 humanized *fragment* with the addition of constant regions to make the full-length antibody not occurring until after transplantation had taken place.

[109] Second, there was no evidence to support Amgen's assertion in its written argument that the PSA "would have known that in order to have the 'parental 5G1.1' antibody used in paragraph [0192] [they] <u>needed</u> to replicate Example 4, the HCDR-3 would need to be restored in the place of the TPO mimetic peptide graft in the 'antibody framework' '5G1.1', necessarily making eculizumab" [emphasis added]. There is no discussion in US972 of using a reverse cloning approach to obtain the "parental 5G1.1" for the test assays of paragraphs [0192] and [0193].

[110] In my view, this late-breaking argument based on paragraphs [0192] and [0193] of US972 is insufficient without further supporting evidence to establish on a balance of

probabilities that US972 (with its incorporated US245 reference) meets the disclosure requirement for anticipation.

[111] For all these reasons, I cannot find that claim 1 is anticipated by US972.

[112] As claim 2 depends from claim 1, and relies on the sequences claimed in claim 1, claim 2 would likewise not be anticipated by US972.

VIII. **Obviousness**

[113] Section 28.3 of the *Patent Act* requires that the subject matter of a claim in an application for a patent in Canada must not have been obvious on the claim date to a PSA having regard to the state of the art. Obviousness is a difficult test to satisfy because it necessitates showing that the PSA would have come directly and without difficulty to the invention, without the benefit of hindsight: *Bridgeview Manufacturing Inc v 931409 Alberta Ltd (Central Alberta Hay Centre)*, 2010 FCA 188 [*Bridgeview*] at para 50.

[114] The Supreme Court of Canada in *Sanofi* set out a four-step approach to an analysis of obviousness, as follows (para 67):

> (1) (a) Identify the notional "person skilled in the art";
>
> (b) Identify the relevant common general knowledge of that person;
>
> (2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;

(3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed;

(4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

[115] In addition, for areas of endeavour where advances are often won by experimentation, an "obvious to try" analysis may be appropriate to take into consideration at the fourth step of the obviousness inquiry. The critical question is whether it "was more or less self-evident to try to obtain the invention" having regard to the following non-exhaustive factors, while noting that "[m]ere possibility that something might turn up is not enough" (*Sanofi* at paras 66, 68-69):

1. Is it more or less self-evident that what is being tried ought to work? Are there a finite number of identified predictable solutions known to persons skilled in the art?

2. What is the extent, nature and amount of effort required to achieve the invention? Are routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine?

3. Is there a motive provided in the prior art to find the solution the patent addresses?

[116] However, the Court must be cautious when approaching the obvious to try analysis as it remains as only one factor amongst many that may assist in the obviousness inquiry: *Bristol Myers Squibb Canada Co v Teva Canada Limited*, 2017 FCA 76 [*Atazanavir*] at para 38; *Sanofi* at para 64. The Court favours "an expansive and flexible approach that would include 'any secondary considerations that [will] prove instructive'": *Sanofi* at para 63; *Atazanavir* at paras 61-62.

[117] The overall analysis is to be flexible, contextual, expansive, and fact-driven: *Apotex Inc v Pfizer Canada Inc*, 2019 FCA 16 at para 39; *Amgen Inc v Pfizer Canada ULC*, 2020 FCA 188 at para 5; *Western Oilfield* at para 109; *Biogen* at para 143. The focus of the analysis centers on whether the distance between two points in the development of the art (the state of the art and the inventive concept) could have been bridged by the PSA without inventiveness, by using only their CGK: *Atazanavir* at para 65; *Merck Sharp & Dohme Corp v Pharmascience Inc*, 2022 FC 417 [*Pharmascience*] at para 156; *Packers Plus Energy Services Inc v Essential Energy Services Ltd*, 2019 FCA 96 at para 32; *Ciba Specialty Chemicals Water Treatments Limited v SNF* Inc, 2017 FCA 225 [*Ciba*] at para 62.

A. *The PSA and their CGK*

[118] The PSA and their CGK were discussed at paragraphs [44] through [50] of these reasons. I adopt the same findings on these aspects for my obviousness analysis.

B. *Inventive Concept*

[119] The inventive concept has been described as not materially different from "the solution taught by the patent": *Atazanavir* at para 75; *Shire* at para 76. Its identification follows from and is informed by, claims construction, although it serves a different purpose: *Shire* at para 75. Claims construction occurs before any assessment of the validity of the claims; its purpose is to interpret and determine the scope of the claims and the protection afforded by the patent. Identification of the inventive concept occurs within the assessment of the validity of the claims. Its purpose is to determine what, if anything, makes the claims, as construed, inventive: *Shire* at paras 75-76; *Pharmascience* at para 168; *Takeda* at para 187.

[120] The parties generally agreed as to the inventive concept of the claims of the 810 Patent. All experts opined that the inventive concept of claim 1 was an antibody that binds C5 with a heavy chain consisting of SEQ ID NO:2 and a light chain consisting of SEQ ID NO:4, although Alexion's experts Dr. Tessier and Dr. Casadevall opined that the binding to C5 was selective (Bertelli, Ex19, para 161; Tessier, Ex29, para 74; Tessier DX, TT 890:6-15; Casadevall, Ex24, paras 147-149).

[121] As I have construed the words "binds C5" in claim 1 to refer to selective binding, the interpretation of this element of the claim must take on the same meaning in the inventive concept. However, the parties agree that nothing turns on this distinction.

[122] Although all essential elements must be considered in the obviousness analysis (*Pharmascience Inc v Bristol-Myers Squibb Canada Co*, 2022 FCA 142 at para 59), I agree with Amgen that as the antibody of claim 1 has been identified in the 810 Patent as eculizumab and eculizumab was known by the claim date, as a matter of CGK, to selectively bind to C5 (Casadevall CX, TT 743:7-24; Casadevall, Ex24, para 85), the inventive concept of claim 1 can also be characterized as the identification of eculizumab's heavy chain and light chain sequences as SEQ ID NO:2 and SEQ ID NO:4, respectively.

[123] As set out earlier, claim 2 is directed to a pharmaceutical composition comprising the antibody of claim 1 (*i.e.*, eculizumab) and a carrier. The inventive concept of claim 2 is accordingly the formulation of the antibody of claim 1 into a pharmaceutical composition so that

it can be delivered to a patient and provide the intended therapeutic effect (Tessier, Ex29, para 76).

C. *State of the Art*

[124] To ascertain the "state of the art" against which the inventive concept is to be compared, for the third part of the *Sanofi* test, the Court may consider any prior art within the public domain relied upon by the parties: *Ciba* at paras 56-60. This is different than the prior art at large: *Ciba* at para 60. While the choice of prior art alleged to be closest to the purported invention is in the hands of the party alleging obviousness, the state of the art may include other prior art identified by a party as being relevant to the purported invention, the motivations of the PSA, or art that is considered to teach away from the direction of the invention: *Apotex Inc v Janssen Inc*, 2021 FCA 45 at para 25; *Pharmascience* at para 160; *Takeda* at para 199. At this step of the analysis, it is not important to consider whether the prior art would have been located by a PSA in a reasonably diligent search, although this might come into play at step 4 of the obviousness analysis when determining whether the uninventive PSA would combine that prior art with other prior art to make the claimed invention: *Hospira Healthcare Corporation v Kennedy Trust for Rheumatology Research*, 2020 FCA 30 at para 86.

[125] While Amgen asserts that the combinations of either US972 and US245, or US245 and WO 97/11971 [WO971] render claim 1 obvious, the parties referred to a broader scope of prior art, which is summarized below.

(1) Early Antibody engineering publications relating to 5G1.1 and h5G1.1

[126] The earliest publications relating to API's antibody engineering development work include the paper by Thomas TC et al, "Inhibition of complement activity by humanized antibody that binds C5 and single-chain Fv" (1996) 33 Mol Immunol 1389-401 [Thomas 1996] (Thomas, Ex9, FC88) and US245.

[127] US245 (Ex7, FC51), discussed earlier, was filed before Thomas 1996 but was published after. It disclosed the preparation of the murine monoclonal antibody referred to as "5G1.1" and other anti-C5 antibody fragments and molecules prepared from 5G1.1, including humanized fragments. It provides the sequences for the V_L and V_H of the murine 5G1.1 antibody and various 5G1.1 humanized scFv fragments, a murine 5G1.1 scFv fragment, chimeric and humanized light chain sequences and chimeric and humanized "Fds", containing the variable heavy chain and CH1 sequence of a Fab (Tessier, Ex29, para 108). It does not disclose any full-length humanized antibodies, or any partial sequences of full-length humanized antibodies (Casadevall, Ex24, para 235). US245 states generally that matched pairs of the variable regions of the "various antibody molecules, Fds, and light chains ... may be combined with constant region domains by recombinant DNA or other methods known in the art to form full length antibodies" and that "[p]articularly preferred constant regions for this purpose [were] IgG constant regions, which may be unaltered, or constructed of a mixture of constant domains from IgGs of various subtypes, e.g., IgG1 and IgG4" (col 45:25-33). It refers to the CH1 regions of Fd fragments, which appear to correspond to IgG1 CHI sequences (Casadevall, Ex24, para 234).

[128] US245 was referenced by Alexion in a 2002 press release as covering "the composition and use of Alexion's lead drug candidates, eculizumab (formerly known as 5G1.1) and pexelizumab, as well as other antibodies that bind to C5 and effectively inhibit its inflammatory activity" (Alexion 2002, Ex5, FC115).

[129] Thomas 1996 reported on API's humanization of the murine 5G1.1 antibody by grafting the variable CDRs of murine 5G1.1 onto human framework regions. The publication disclosed results demonstrating that all humanized h5G1.1 constructs (humanized Fab and scFv fragments) bound C5 and blocked its cleavage and disclosed the variable region amino acid sequences of murine 5G1.1 and the humanized fragments, including their CDRs. It also disclosed the construction of one full length h5G1.1 antibody made from one of the humanized fragments comprising an IgG4 constant region that also bound C5 with "similar" avidity to murine antibody, and blocked C5 cleavage (pages 1396 and 1399). The human IgG4 isotype was chosen in part because it did not activate human complement (page 1399). The paper concluded that "[l]ittle information [was] available on the immunogenicity of CDR-grafted antibodies in humans" but noted that "introduction of murine amino acids in the framework regions was not essential for maintenance of high affinity binding to C5" and that the h5G1.1 antibody was therefore "likely to be minimally immunogenic in patients" (page 1399).

(2) Chemical Abstract Service [CAS] Listing

[130] In 1999, API deposited what it thought was the correct amino acid sequence for eculizumab with the CAS without any obligation of confidence (Ex31, Tabs 1A, 1C; Agreed Statement of Facts [ASF]: 289, 290). Although the sequence included significant errors, it also

included recognizable portions in the CH1 constant region and the hinge region, which were characteristic of IgG2, and in the CH3 and CH4 constant regions, which were characteristic of IgG4 (Tessier CX, TT (5B) 16:10-17:13, 17:22-18:6). The sequence was initially filed under "5G1.1" but the name "eculizumab" became attributed to the CAS listing before March 15, 2007 (ASF: 37-38, 42, 291).

(3) Clinical Art

[131] As early as 2002, there were publications specifically referring to eculizumab and API's clinical studies involving eculizumab (see for example, Kaplan M, "Eculizumab Alexion" (2002) 3:7 Current Opinion in Investigational Drugs 1017-1023 [Kaplan 2002] (Kaplan, Ex12, FC319)).

[132] Kaplan 2002 referred to "[e]culizumab (5G1.1)" as a humanized C5 inhibitory monoclonal antibody "under development by Alexion Pharmaceuticals Inc" that "prevents the cleavage of human complement component C5 into its pro-inflammatory components" (page 1017). It cited to Thomas 1996 in its discussion of the synthesis of humanized 5G1.1, Fab and scFv molecules (pages 1018, 1022) and referenced US245 as covering the composition of eculizumab, along with pexelizumab and other C5-binding anti-inflammatory antibodies (page 1020). Kaplan 2002 stated that eculizumab was in phase II clinical trials for a "variety of chronic inflammatory conditions" and described eculizumab as a potential treatment for rheumatoid arthritis, systemic lupus erythematosus (autoimmune disease), and nephritis (page 1018).

[133] In 2004, Hillmen P et al, "Effect of Eculizumab on Hemolysis and Transfusion Requirements in Patients with Paroxysmal Nocturnal Hemoglobinuria" (2004) 350:6 N Engl J

Med 552-559 [Hillmen 2004] (Hillmen, Ex10, FC64) reported on a small-scale, 12-week pilot study of 11 PNH patients treated with the drug eculizumab. The paper concluded that eculizumab was "safe and well tolerated in patients with PNH" and that it reduced "intravascular hemolysis, hemoglobinuria, and the need for transfusion, with an associated improvement in the quality of life" (page 552). It described eculizumab as "a recombinant humanized monoclonal antibody that was designed to block the activation of terminal complement components," citing to Thomas 1996 and an earlier paper (pages 553 and 559).

[134] Hillmen 2004 was described as a hallmark paper in the field that was received with "excitement" by the hematology community when it was published (Boulad, Ex12, para 105; Tessier DX, TT 892:15-23) and later became part of the CGK (Boulad, Ex12, para 105; Tessier, Ex29, para 127; Casadevall CX, TT 733:5-15).

[135] The pilot study reported in Hillmen 2004 was followed by an extension study (Hill A, et al, "Sustained Response and Long-term Safety of Eculizumab in Paroxysmal Nocturnal Hemoglobinuria" (2005) 106:7 Blood 2559-2566 [Hill I 2005]) (Hill, Ex12, FC312) investigating the long-term safety and efficacy of eculizumab in the 11 patients studied by Hillmen. Hill I 2005 reported that eculizumab continued to be safe and well tolerated showing sustained reductions in hemolysis and blood transfusions and continued improvement in quality of life.

[136] Later the same year, an interview with Hill was reported in Clinical Advances in Hematology & Oncology [Hill II 2005] (Hill, Ex12, FC313). In the interview, Hill identified

eculizumab as “a monoclonal antibody that blocked the complement system at protein C5” that “should be effective in preventing hemolysis” and which she had “little doubt” would be effective for treating PNH. She noted that two Phase III trials (TRIUMPH and SHEPHERD) were underway and that researchers were “eagerly awaiting the results” (Hill II 2005 at page 850; Boulad, Ex12, paras 145-147).

[137] The promising results of eculizumab were also discussed in the American Society of Hematology publication, Rosse WF, “Immune-Mediated Hemolytic Anemia” (2004) Hematology 48-62 [Rosse 2004]) (Rosse, Ex12, FC324) which included a report by Hillmen on his findings in PNH and his work with “a humanized monoclonal antibody against C5” that had showed a “remarkable effect in controlling the manifestations of the disease” (page 48). In the section on Hillmen’s work, it referred to eculizumab as “a humanized chimeric antibody against C5 with a completely nonfunctional Fc domain” (page 53).

[138] US Patent Application No. 2005/0191298, owned by API, titled “Method of treating hemolytic disease” [US298] (US298, Ex19, FC280) was also published in 2005, and disclosed a method of treating PNH “by administering a compound that binds to, or otherwise blocks, the generation and/or activation of one or more complement components” (at para [0003]). US298 disclosed as one embodiment, “an anti-C5 antibody selected from the group consisting of h5G1.1-mAb (eculizumab), h5G1.1-scFv (pexelizumab) and other functional fragments of h5G1.1” (at para [0012]). It stated that particularly useful anti-C5 antibodies were h5G1.1-mAb, h5G1.1-scFv and other functional fragments of h5G1.1 and referred to methods for the preparation of these antibodies as being described in US245 and Thomas 1996, while noting that

"h5G1.1-mAb is currently undergoing clinical trials under the tradename eculizumab" [at para [0052]). In its examples, it described an 11-patient pilot study in PNH patients involving eculizumab and an extension study of those patients, which corresponded to the studies reported in Hillmen 2004 and Hill I 2005 (Tessier, Ex29, para 120; Casadevall, Ex24, para 212; Boulad, Ex12, para 166).

(4) Other API art referencing "eculizumab", "5G1.1" or "h5G1.1"

[139] Shortly after Thomas 1996, in 1997, a research group at API that included some of the same scientists named on Thomas 1996 reported on separate work relating to the humanization of porcine vascular cell adhesion molecule [VCAM] specific monoclonal antibodies for xenotransplantation (the transplant of non-human organs into human subjects) (Mueller JP et al, "Humanized Porcine VCAM-specific monoclonal antibodies with chimeric IgG2/IgG4 constant regions block human leukocyte binding to porcine endothelial cells" (1997) 34:6 Mol Immunol 441-452) [Mueller 1997] (Ex19, FC292) and WO 97/11971, titled "Porcine Cell Interaction Proteins" [WO971] (Ex19, FC291)). Mueller 1997 and WO971 described anti-porcine VCAM antibodies with IgG4 and hybrid IgG2/G4 constant regions.

[140] In Mueller 1997, the authors described the hybrid IgG2/G4 constant region as an alternative to altering the specific residues known to mediate complement fixation and Fc receptor binding (page 446). They referred to human antibodies of the IgG4 isotype as being devoid of complement activity and those of the IgG2 isotype as not activating complement or binding Fc receptors (page 446; Tessier, Ex29, para 99). Both Mueller 1997 and WO971 described the IgG2/G4 hybrid as including the CH1 constant region domain and the hinge region

from the IgG2 isotype joined to the CH2 and CH3 constant region domains of the IgG4 isotype. Two h5G1.1 antibodies with corresponding IgG4 and IgG2/G4 heavy chain constant regions were used as negative control antibodies in the experiments.

[141] Mueller 1997 disclosed that the VCAM antibodies with IgG4 heavy chain constant region bound to Fc receptors (FcγR1, FcγRII and FcγRIII) whereas those with a hybrid IgG2/G4 heavy chain constant region did not bind Fc receptors (pages 447-448; Bertelli, Ex19, para 221). It stated that the IgG2/G4 hybrid antibody design "should prove useful in humanization of other antibodies intended for human use where elimination of Fc [receptor] binding and [complement] activation may be desirable" (page 451).

[142] WO971 included the complete amino acid sequences for the heavy chain of the VCAM antibodies with a IgG2/G4 hybrid heavy chain constant region and in a separate figure, the variable region sequences. From this, Dr. Bertelli opined that the PSA would have been able to determine the amino acid sequence of the IgG2/G4 hybrid heavy chain constant region (Bertelli, Ex19, para 118).

[143] In US972, discussed earlier, API scientist Katherine Bowdish filed a patent application disclosing the preparation of antibody constructs for transporting biologically active peptides. Example 4 described the preparation of an antibody construct with a TPO peptide transplanted in place of the heavy chain CDR3 of a 5G1.1 antibody scaffold. US972 referenced US245 for construction of the 5G1.1 antibody framework. The sequence of the light chain and the heavy

chain of the final 5G1[.1] + peptide produced was disclosed and included an IgG2/G4 heavy constant region.

[144] API sought protection for an antibody with an IgG2/G4 constant region in two patent applications filed in 2004: WO 2005/007809 [WO809] (Ex19, FC297) and WO 2004/108158 [WO158] (Ex 19, FC295). However, neither related to complement inhibition or anti-C5 activity (Tessier, Ex29, paras 142, 143, 146; Casadevall, Ex24, paras 328, 331).

[145] In 2005, a joint paper with API scientists (Tacken PJ et al, "Effective Induction of Naïve and Recall T-cell Responses by Targeting Antigen to Human Dendritic Cells via a Humanized anti-DC-SIGN Antibody" (2005) 106(4) Blood 1278-1285 [Tacken 2005] (Tacken, Ex19, FC298)), reported on the humanization of an anti-DC-SIGN antibody with an IgG2/G4 constant region. Tacken 2005 described the antibody as having "humanized variable heavy and variable light regions" that were "genetically fused with a human hybrid IgG2/IgG4 constant domain, and a human kappa chain constant domain", citing to Mueller 1997 for the human hybrid IgG2/G4 constant domain (page 1279).

[146] The paper referred to "[a]n isotype control antibody, h5G1.1-mAb (5G1.1, eculizamab; Alexion Pharmaceuticals) containing the same IgG2/IgG4 constant region [as in Mueller 1997] [that was] specific for the human terminal complement protein C5", citing to Thomas 1996 (pages 1279 and 1285). In the discussion, Tacken 2005 referenced Mueller 1997 as previously showing that "the human hybrid IgG2/IgG4 constant region prevents antibodies from binding to Fc receptors" (page 1280).

[147] While Tacken 2005 referred to the control antibody as "eculiz**a**mab" [emphasis added], I agree with Dr. Bertelli, the PSA would have viewed this as a misspelling and would have recognized the molecule being referenced as eculizumab (Bertelli DX, TT 458:16-459:1). As confirmed by Dr. Bell, there was no therapeutic development product from Alexion named eculizamab (Bell CX, TT 168:23-169:6).

D. *Differences between the State of the Art and the Inventive Concept*

[148] From the state of the art, the PSA would have known that API had a drug named eculizumab, which was associated with the murine monoclonal antibody 5G1.1 and its humanization; that eculizumab was selective for C5; and that it was being used to treat patients with PNH with promising results. However, none of the prior art disclosed heavy chain and light chain sequences for eculizumab. Nor was there disclosure of any anti-C5 antibody that had both an amino acid sequence for its light chain that was the same as SEQ ID NO:4 and an amino acid sequence for its heavy chain that was the same as SEQ ID NO:2.

[149] While amino acid sequences for the variable regions of humanized fragments of 5G1.1 had been reported in US245 and Thomas 1996, amino acid sequences for the heavy chain constant regions of IgG subtypes were known and available in computer databases, and amino acid sequences for hybrid heavy chain constant regions had been reported in the broader prior art, there was no direct connection between these sequences and eculizumab.

[150] Although Amgen asserts that there are no differences between the state of the art and the inventive concept as the combinations of either US245 and US972, or US245 and WO917 would

have led the PSA to the claimed sequences, this requires an assessment under step 4 of the *Sanofi* test. The outstanding issue is whether the PSA would have combined these references and if so, would have been able to arrive at the claimed sequences without inventiveness.

E. *Would the Differences have been Bridged Without Inventiveness?*

[151] The parties take different approaches to the starting point for step 4 of the analysis under *Sanofi* and how the PSA would have been motivated from the state of the art.

[152] As its primary position, Alexion characterizes the analysis as whether a PSA looking to create an antibody that binds C5, whether selectively or not, would have been led to the claimed sequences. As its secondary position, it considers whether a PSA specifically looking for the sequence of eculizumab would have been led to the claimed sequences. Amgen asserts that the latter is the correct question. I agree with Amgen.

[153] I note that the evidence from Alexion's experts was not consistent on this issue. While the experts opined on whether it would have been obvious for the PSA to design a new anti-C5 antibody with the sequences of claim 1, they also acknowledged the importance of the Hillmen 2004 reference and that from this reference, the PSA would have been specifically interested in the antibody referred to in Hillmen 2004 as eculizumab (Casadevall, Ex24, para 201) and of finding its sequence (Tessier, Ex29, paras 183, 160).

[154] Indeed, the PSA would have known from both the prior art and the skilled clinician on the team that API had conducted significant development work already, that they had made a

humanized antibody and formulated it into a drug called eculizumab that was already in clinical trials for the treatment of patients with PNH, and that preliminary clinical studies had shown promising results (Bertelli, Ex19, para 159). With this head start by API, in my view, the PSA would not have been looking to create a new, unrelated anti-C5 antibody; rather, they would have sought to minimize the pitfalls and struggles associated with antibody design (Casadevall, Ex24, paras 170-177, 181) by looking for the sequence of eculizumab.

[155] Relying on the evidence of Dr. Tessier and Dr. Casadevall, Alexion asserts that even if the PSA had started with this question, they would have been directed to Thomas 1996 for the sequence of eculizumab, and stopped there, as they would have thought that eculizumab was comprised of the variable CDR sequence disclosed in Thomas 1996 constructed with an IgG4 constant region (Tessier, Ex29, paras 163-166; Casadevall, Ex24, para 360). Alexion places great emphasis on the reference to Thomas 1996 that was made in Hillmen 2004 when describing eculizumab as "a recombinant humanized monoclonal antibody that was designed to block the activation of terminal complement components" and of similar references to Thomas 1996 that were made in Kaplan 2002, Hill I 2005, and US298, among other references (Casadevall, Ex24, paras 204, 362-366; Tessier, Ex29, paras 46(a), 163, 164).

[156] In cross-examination, Dr. Bell stated that the reference to Thomas 1996 in Hillmen 2004 was not intended to provide any information on the sequence of eculizumab, and that the entire sequence for eculizumab was not disclosed in Thomas 1996 (Bell CX, TT 163:19-24). Rather, he stated that Thomas 1996 was cited as support for the activity of the variable region of the humanized 5G1.1 antibody to block C5 (Bell CX, TT 165:19-166:4, 166:16-168:5).

[157] Alexion asserts that Dr. Bell's comments are irrelevant as it is only the PSA's perspective that is important. They rely on the evidence of Drs. Tessier and Casadevall who opine that the PSA would rely on the repeated reference to Thomas 1996, along with the rationale given in Thomas 1996 for an IgG4 antibody that does not activate human complement, and which showed binding to human C5 with similar avidity to the original murine antibody (Tessier, Ex29, paras 164-165; Casadevall, Ex24, para 366).

[158] In essence, Alexion's argument is that its own clinical art through reference to Thomas 1996 was directing the PSA towards Thomas 1996 (and away from other prior art or inquiries) for the sequence of eculizumab. However, I do not agree that the citations to Thomas 1996 go this far.

[159] The references to Thomas 1996 must be read in context. First, the references in Hillmen 2004, Kaplan 2002, Hill I 2005, and US298 are made in documents that are directed to the clinician who is concerned with the ability of the antibody to inhibit the activity of C5, not the sequence of the antibody. Second, none of the passages suggest that Thomas 1996 discloses the sequence of eculizumab. Nor does Thomas 1996 say this.

[160] As acknowledged by Dr. Casadevall, Thomas 1996 is an ancestry document that refers to the origins of the variable region humanization work on 5G1.1 and the confirmation of its anti-C5 activity (Casadevall CX, TT 682:1-8).

[161] While Thomas chose to produce an intact humanized 5G1.1 antibody as an IgG4 isotype because it would not activate complement, as explained by Dr. Bertelli, the PSA would have known that there were still some questions left unanswered, including whether the antibody provoked any quasi-effector function by stimulating the immune cells through Fc gamma receptor binding (Bertelli DX, TT 448:24-449:19).

[162] However, even if the PSA viewed Thomas 1996 in this manner, this does not establish that the PSA would have been led instead to the sequences of claim 1 of the 810 Patent through the combinations proposed by Amgen.

[163] Indeed, while it is possible to mosaic or combine prior art references that are not part of the CGK, the party alleging obviousness must establish that the PSA would have thought to combine those references: *Pharmascience Inc v Teva Canada Innovation*, 2022 FCA 2 at para 33; *Usinage Pro-24 Inc v Valley Blades Ltd*, 2025 FCA 4 [*Usinage*] at para 38. A PSA cannot simply link one piece of prior art with another, unless it would be uninventive to do so: *Camso Inc v Soucy International Inc*, 2019 FC 255 at 125.

[164] Amgen asserts that the PSA would have been directed to US245 as it was an API patent involving 5G1.1 that was repeatedly referenced in API's prior art with reference to eculizumab and identified in Alexion 2002 as being the cornerstone to eculizumab's development. They assert that as eculizumab was known to be a drug of API and associated with 5G1.1 and h5G1.1, the PSA would have paid attention to references that referred to these constructs and to the particular researchers who participated in studies involving 5G1.1 and h5G1.1, including the

US972 and WO971 references, each of which were also cross-referenced to US245. As the PSA was motivated to find the sequence of eculizumab, the PSA would have looked to those references with the most complete antibody sequences, which would have taken the PSA to US972 or WO971.

[165] Alexion does not take issue with US245 being prior art of interest but disagrees that Amgen has established that the PSA would have been motivated to combine either US972 or WO971 with US245.

[166] Although Dr. Tessier took issue with the relevance of US972 in his report, he stated that a PSA looking to create an antibody that binds C5 would have had four paths to choose from arising from the collection of prior art in the proceeding, one of which included combining the IgG2/G4 constant region of the 5G1[.1] + peptide antibody disclosed in Example 4 of US972 with the variable region of one of the fragments or scFv molecules from US245. The others he identified as: an IgG4 antibody with the variable region from Thomas 1996; the antibody fragments disclosed in US245 with an IgG4 constant region, or one of the scFv molecules without a constant region; or the antibody of the CAS Listing (Tessier, Ex29, para 162; Tessier DX, TT 910:22-912:15).

[167] However, Dr. Tessier asserted that the PSA would not have chosen to pursue the combination of US972 with US245, especially in the face of Thomas 1996 (Tessier CX, TT 1045:2-1046:13).

[168] As highlighted by Dr. Tessier, and conceded by Dr. Bertelli, US972 did not disclose any anti-C5 activity, including for the product antibody from Example 4, which had an IgG2/G4 constant region (Tessier, Ex29, para 174; Bertelli CX, TT 556:15-18). Nor was their any prior art reporting data on an IgG2/G4 antibody's ability to bind C5 (Tessier, Ex29, para 176, 234; Bertelli CX, TT 545:15-25).

[169] US972 did not disclose whether the antibody made in Example 4 had any immunologic effects (Bertelli CX, TT 556:19-22) as this was not the focus of the application. Indeed, US972 was directed at transplanting and stabilizing mimetic peptides in place of the CDR3 from an antibody framework. The antibodies produced were not expected to retain the same activity or binding without the CDR3 (Bertelli DX, TT 413:10-16; Tessier CX, TT 1050:2-10); nor was there any suggestion that they were made for their anti-C5 activity.

[170] Thus, even if I accept that the PSA would be looking to broader API publications, without there being any anti-C5 activity studies in US972, or a direct connection between the product of Example 4 and eculizumab, I am not satisfied the PSA would have considered US972 to be a reference of particular interest to pursue.

[171] Contrary to the assertions of Amgen, I am not convinced that the PSA looking for the sequence of eculizumab would be interested in all publications that included the term "5G1.1" or "h5G1.1", especially as the nomenclature 5G1.1 and h5G1.1 was also associated with pexelizumab and other C5-binding anti-inflammatory antibodies, which would be of lesser interest (see for example, US298 and Kaplan 2002). Indeed, while Dr. Tessier identified

US972/US245 as a potential pathway he did so only when considering the options available to the PSA looking broadly to design a new anti-C5 antibody based on the prior art that had been produced, not from the perspective of a PSA who was looking for the sequence of eculizumab. By the time of US972, API had moved away from using “5G1.1” and was referring to its clinical drug product as eculizumab.

[172] Although the 5G1[.1] + peptide product of Example 4 would have been understood to be a humanized antibody from the sequences disclosed in Figures 13A and 13B, as admitted by Amgen, these sequences would not be of interest to a PSA unless there was some perceived connection between the product of Example 4 and eculizumab.

[173] Similarly, while US972 refers to US245 in Example 4, US245 does not refer to US972. In other words, the PSA would need to have an interest in US972 to make the connection between this reference and US245.

[174] If the PSA did not pursue the combination of US972 and US245, Amgen asserts that the PSA would have been led to the sequences of claim 1 of the 810 Patent through the combination of the sequence for the IgG2/G4 hybrid heavy chain constant region disclosed in WO971 and the sequence for the humanized 5G1.1 fragment of Example 11(12), SEQ ID NO:20 from US245.

[175] Dr. Bertelli opines that the PSA would have been led beyond the teachings of Thomas 1996 to WO971, which recognizes the advantages of an IgG2/G4 hybrid heavy chain that does not activate complement activation or bind to Fc receptor (Bertelli, Ex19, paras 186, 216-221;

Bertelli DX, TT 449:8-453:11). He refers to additional prior art that also identified eculizumab as having a hybrid IgG2/G4 heavy chain constant region (*i.e.*, Tacken 2005 and the CAS Listing) or refers to eculizumab as an antibody with a completely nonfunctional Fc domain (*i.e.*, Rosse 2004) (Bertelli, Ex19, para 214).

[176] Amgen asserts that the CAS listing is relevant and must be considered for five reasons. First, it asserts that it is relevant to whether eculizumab has a heavy chain constant region that is a IgG2/G4 hybrid. Second, it argues that the CAS Listing puts API's other prior art disclosures in context – in other words, if in February 1999 Alexion believed it had already publicly disclosed the full sequence of eculizumab, it follows that it would have thought that it did not need to separately disclose the sequence, and the reference in Hillmen 2004 to Thomas 1996 was likely for a different purpose. Third, it asserts that the CAS Listing identifies a further path available to the PSA (Tessier, Ex29, para 162) which was only complicated by API's own errors, which could have been corrected by inquiring of CAS or API. Fourth, in view of the ability to correct the sequence, it contends that it is relevant to whether, as a legal matter, the correct eculizumab sequence is actually part of the prior art. Last, Amgen asserts that the CAS Listing is relevant to the patent bargain and whether API should maintain protection over a sequence it intended to disclose to the public.

[177] However, some of this is conjecture (the second reason asserted), or raises arguments that extend beyond Amgen's pleading (the fourth and fifth reasons asserted). Notably, there is no longer any section 53(1) allegation or anticipation argument relating to the CAS Listing in Amgen's Statement of Defence as this was removed by amendment. Nor is there any legal basis

cited to support Amgen's fifth proposition: see also *Rovi Guides, Inc v Videotron Ltd*, 2024 FCA 125 at para 82.

[178] I agree that the evidence indicates that API wanted to disclose the sequence of eculizumab to the public as early as 1999 (Ex31, Tabs 1A, 1C). However, by depositing a sequence that had errors, it did not do so.

[179] Even though Dr. Tessier acknowledged that the PSA could have made further inquiries of CAS or API regarding the sequence (Tessier CX, TT (5B) 18:1-20:20), none of the experts opined that a PSA would have done this. Rather, instead all experts agreed that the sequence had significant error and that they would have moved on from the sequence and looked at other prior art (Bertelli CX, TT 591-2-7, 596:11-22; Tessier, Ex29, paras 178, 232; Casadevall, Ex24, para 443).

[180] Each of the experts indicated that there were portions of the heavy chain constant region sequence (CH1 and hinge) that would have been recognizable as being from the IgG2 isotype, while other portions from the CH3 and CH4 heavy chain constant regions were characteristic of IgG4 (Bertelli, Ex19, para 214(c); Bertelli CX, TT 594:6-19; Tessier, Ex29, paras 149, 178; Tessier CX, TT (5B) 17:1-13, 22-18:6). As admitted by Dr. Tessier, this would have indicated to the PSA that eculizumab could have a heavy chain that was an IgG2/G4 hybrid (Tessier, Ex29, para 178; Tessier CX, TT (5B)18:1-24), thereby, in my view, making references such as Tacken 2005 more relevant. However, the evidence does not establish that the PSA would have arrived at the sequences of claim 1 of the 810 Patent using the CAS Listing alone.

[181] Although Dr. Bertelli suggested during cross-examination that if the errors from the CAS Listing were removed, the PSA would have been left with the heavy chain constant region sequence for eculizumab, he had to admit that he had not identified the specific errors in the sequence, nor conducted any comparison of the sequence in the CAS Listing with the sequences in the 810 Patent or conducted an examination of the variable region (Bertelli CX, TT 594:25-596:22).

[182] Dr. Tessier, who did conduct this comparison, described the differences in the heavy chain as "significant" and noted additional differences with the light chain sequence. He doubted that the PSA would be able to identify all the errors, particularly in view of the possible hybrid structure of the heavy chain, opining that the PSA would have to make different iterations of the antibody with various insertions, deletions and substitutions to better evaluate the sequence (Tessier, Ex29, paras 179-180).

[183] Indeed, there was insufficient evidence before me as to the full amount of work that would have been required to get from the CAS Listing (with errors) to the sequences claimed in the 810 Patent, and no evidence to establish that the PSA would have pursued the CAS Listing to obtain a corrected sequence.

[184] As highlighted by Alexion, the obviousness analysis concerns what the PSA would have done in light of the state of the art and their CGK. It is not sufficient to establish what the PSA could have done: *Usinage* at para 33.

[185] With respect to WO971, there is no direct association between the IgG2/G4 hybrid heavy chain constant region used on the antibodies in that study and eculizumab. However, as noted by Dr. Bertelli, Tacken 2005 cites to the related article Mueller 1997 and identifies the IgG2/G4 hybrid heavy chain constant region of the eculizumab hG51.1 control used in Tacken 2005 as having the same IgG2/G4 constant region discussed in Mueller 1997 (Bertelli RX, TT 604:19-605:6).

[186] Although the evidence relating to Tacken 2005 was thin, I am satisfied that Tacken 2005, which specifically refers to eculizumab, *albeit* misspelled, would have been uncovered through searches conducted by the PSA for eculizumab. From Tacken 2005 and the CAS Listing, it would have been reasonable for the PSA to believe that the heavy chain constant region of eculizumab was at least being tested as a IgG2/G4 hybrid.

[187] However, this still does not establish that the PSA would be led to WO971 as Tacken 2005 cites to Mueller 1997 not WO971. Nor does it establish that the PSA would be led to the combination of WO971 and US245 as Tacken 2005 also cites to Thomas 1996 not to US245.

[188] Further, both Mueller 1997 and WO971 refer to a different antibody system that does not test for C5 binding (Tessier CX, TT 1053:5-19). While there was an h5G1.1 control with an IgG2/G4 heavy chain used in the WO971 patent application, there was no disclosure of that control having anti-C5 activity. Rather, WO971 refers only to the h5G1.1 IgG4 control as having this function (Tessier, Ex29, paras 100, 227; Tessier CX, TT 1054:10-1055:6).

[189] Dr. Bertelli refers to API's prior art relating to the hybrid IgG2/G4 heavy chain constant region (*i.e.*, Mueller, WO971, Tacken 2005, WO158, WO809) as showing that a hybrid constant region did not interfere with antibody function (Bertelli, Ex19, para 215; Bertelli DX, TT 459:16-461:11). However, he admitted that the binding data from those publications did not assay the impact of a hybrid heavy chain constant region on C5 binding (Bertelli CX, TT 545:15-25, 552:20-24, 568:11-16, 575:8-15, 576:18-20).

[190] He opined that the PSA would have preferred to make an IgG2/G4 antibody instead of an IgG4 antibody because they would have known that it was completely devoid of effector function (Bertelli DX, TT 445:21-446:18; see also Bertelli, Ex19, paras 216-221), which, as reported in WO809, provided additional advantages, such as "reduc[ing] the ability of the antibody to elicit inflammatory events such as cell activation, cytokine release and complement activation" (WO809, Ex19, FC297, p. 11; Bertelli, Ex19, para 220). However, again he could not cite to any examples of an anti-C5 antibody where the impact on effector function was studied together with complement inhibition.

[191] Even if I were to accept that the PSA would have considered the sequence for the IgG2/G4 heavy chain constant region in WO971 in addition to an IgG4 constant region, Amgen must still establish that the PSA would have been led to the sequences claimed in claim 1 of the 810 Patent. This requires not only landing on the IgG2/G4 heavy chain constant region from WO971 but also the combination of that sequence with SEQ ID NO:20 from US245.

[192] On the latter point, Amgen relies on the common notation given to the h5G1.1 control molecule in WO971 (CO12), which was also used to describe the fragment of Example 11(12) and SEQ ID NO:20 in US245 (Bertelli, Ex19, paras 185, 193).

[193] According to Dr. Bertelli, due to the commonality in terminology, the PSA would have understood that the h5G1.1 CO12 variable regions (heavy and light chain) used in WO971 are the same as the humanized 5G1.1 CO12 variable regions (heavy and light chain) in SEQ ID NO:20 of US245 (Bertelli, Ex19, para 194). SEQ ID NO:20 therefore would have provided the PSA with the heavy and light chain variable regions sequences of 5G1.1 scFv CO12 to combine with the IgG2/G4 heavy chain constant region sequence from WO971 (Bertelli, Ex19, para 196), which could have been accomplished using common cloning techniques (Bertelli, Ex19, paras 196-199).

[194] As admitted by Amgen, to arrive at the full sequence of claim 1 of the 810 Patent, the PSA must make a connection through the “CO12” notation used in WO971. However, I agree with Alexion, without further information linking the CO12 notation in WO971 with the fragment of Example 11(12) in US245 and its sequence, such a connection would not have been made.

[195] First, the CO12 notation would not have been striking on its own to the PSA. There were multiple designations used throughout the prior art for humanized antibodies and fragments. As noted by Dr. Casadevall, there is no teaching within WO971 as to the “CO12” designation

(Casadevall, Ex24, para 373) and none of the experts could definitively explain what it meant (Bertelli DX, TT 439:23-440:16; Casadevall DX, TT 848:24-849:3).

[196] Second, the art uses the same terminology at times for very different antibodies and antibody fragments (Tessier, Ex29, para 228). Without a specific connection to a sequence in US245, the PSA would not have been able to determine whether or not the sequence of the antibody in WO971 had any connection to the fragments described in US245 and in particular, the fragment of SEQ ID NO:20 (Casadevall, Ex24, para 373).

[197] In my view, there is no clear and convincing evidence that the PSA would have been directed to SEQ ID NO:20 of Example 11(12) of US245. Dr. Bertelli's focus on the CO12 notation is simply a matter of hindsight.

[198] Further, Amgen has failed to satisfy me that any specific sequence from US245 would have been obvious to try in combination with the IgG2/G4 constant region of WO971.

[199] I agree with Alexion, even if the PSA was specifically interested in creating an antibody with an IgG2/G4 constant region, given the number of variants disclosed in US245 and Thomas 1996, there existed many options for the PSA to try without any specific evidence as to how long testing would take, how difficult it would be, or expectation of results.

[200] As highlighted by Dr. Tessier, US245 did not report on the anti-C5 activity of any full-length humanized antibodies, and its data would have been understood to be limited to

non-humanized antibodies and antibody fragments (Tessier, Ex29, para 161; Ex7, FC51, col 9:44-64). Thus, the PSA would have also been left without any specific guidance as to which of the many sequences to try based on functionality and on whether any variant would have anti-C5 activity when constructed with an IgG2/G4 hybrid heavy chain constant region (Tessier, Ex29, paras 181, 211; Tessier DX, TT 904:11-905:15). Further, as explained by Dr. Tessier, while a PSA would be able to identify the V_H and V_L regions of an scFv molecule to combine with respective constant regions, combining with a hybrid heavy chain constant region was not usual or straightforward. Thus, it would not have been clear whether this would be successful and whether there would be desired activity (Tessier CX, TT 1013:15-1014:20).

[201] Admittedly, Amgen's case is based on a paper record. However, there are too many connections to be made and gaps to fill to establish a clear path to the claimed invention.

[202] On the basis of the evidence before me, I cannot conclude that Amgen has met its burden of establishing with clear, compelling, and convincing evidence that claim 1 of the 810 Patent was obvious.

[203] As claim 2 of the 810 Patent relies on the findings of claim 1, it is also my view that claim 2 is not obvious.

IX. **Conclusion**

[204] For all these reasons, Amgen has not established that claims 1 and 2 of the 810 Patent are invalid for either anticipation or obviousness.

[205] As such, the action as it relates to claims 1 and 2 of the 810 Patent is allowed and the Plaintiffs shall be granted a declaration of infringement and an injunction preventing Amgen from manufacturing, using, and selling the Amgen Product in Canada until the expiration date of the 810 Patent. Noting the Federal Court of Appeal's January 9, 2025 Judgment in *JAMP Pharma Corporation v Boehringer Ingelheim (Canada) Ltd*. (A-306-24) varying the Federal Court's Judgment in that case, I shall make the injunction subject to any agreement by the Plaintiffs in writing otherwise.

[206] Alexion has also requested an order for delivery up or destruction at their election of all eculizumab product including, but not limited to, "any intermediates, bulk product, and finished product ... in Amgen's power, possession or control" that would offend the injunction requested. I note that any such provision cannot include product that would otherwise be exempt from infringement by the *Patent Act*; for example, product that would come under subsection 55.2(1) of the *Patent Act*. As Amgen did not contest the inclusion of such a provision in any Judgment if Alexion was successful, and in view of subsection 6(4) of the *PMNOC Regulations*, I see no reason to refuse this request. I shall therefore also include this relief, subject to the caveat noted, as part of my Judgment.

X. **Costs**

[207] As Alexion has been successful, they shall be awarded their costs. The parties advised that they have come to an agreement as to the quantum of costs. Costs shall therefore be awarded in accordance with that agreement.

XI. ***Official Languages Act***

[208] In view of the 24-month stay under paragraph 7(1)(d) of the *PMNOC Regulations*, the timing of this decision will have an impact on the parties. To the extent that paragraph 20(1)(a.1) of the *Official Languages Act* RSC, 1985, c 31 (4th Supp) [OLA] applies to this decision, it is my view that paragraph 20(2)(b) of the OLA is invoked, justifying immediate release of this decision in English (the language in which the matter was argued) with the translation into French to be released at the earliest possible time thereafter.

JUDGMENT IN T-1094-23 AND T-1095-23

THIS COURT'S JUDGMENT is that:

1. The action is granted as it relates to claims 1 and 2 of Canadian Patent No. 2,645,810 [810 Patent].

2. The making, constructing, using, or selling of BEKEMV eculizumab for injection as a 30 mL parenteral solution (10 mg/mL)[Amgen Product] by Amgen Canada Inc. [Amgen] in accordance with New Drug Submissions Nos. 263132 and 273714 would infringe claims 1 and 2 of the 810 Patent, directly and/or indirectly.

3. Unless otherwise agreed to in writing by the Plaintiffs, Amgen as well as its subsidiary and affiliated companies, officers, directors, employees, agents, licensees, successors, assigns and any others over whom Amgen exercises lawful authority are hereby enjoined from the following acts until March 15, 2027, the date when the 810 Patent expires:

    a. making, constructing, using, or selling the Amgen Product in Canada;

    b. offering for sale, marketing, or having the Amgen Product marketed in Canada;

    c. importing, exporting, distributing, or having the Amgen Product distributed in Canada; and

d. otherwise infringing or inducing others to infringe the 810 Patent.

4. Amgen is required to deliver up to the Plaintiffs or to destroy under oath, at the Plaintiffs' election, all eculizumab product, including, but not limited to, any intermediates, bulk product, and finished product thereof, in Amgen's power, possession or control that is not otherwise exempted from infringement under the *Patent Act* that would offend the injunction in paragraph 3.

5. Costs to the Plaintiffs in the amount agreed to by the parties.

"Angela Furlanetto"
Judge

FEDERAL COURT

SOLICITORS OF RECORD

DOCKETS:	T-1094-23 AND T-1095-23
STYLE OF CAUSE:	ALEXION PHARMACEUTICALS, INC., AND ALEXION PHARMA INTERNATIONAL OPERATIONS LIMITED v AMGEN CANADA INC.
PLACE OF HEARING:	TORONTO, ONTARIO
DATE OF HEARING:	JANUARY 27, 2025 TO JANUARY 31, 2025 FEBRUARY 14, 2025
JUDGMENT AND REASONS:	FURLANETTO, J
CONFIDENTIAL JUDGMENT AND REASONS ISSUED:	APRIL 28, 2025
PUBLIC JUDGMENT AND REASONS ISSUED:	MAY 12, 2025

APPEARANCES:

Marian Wolanski Megan Pocalyuko Kelly Zhang Mimoza Gjelaj	FOR THE PLAINTIFFS
Jason Markwell Dino Clarizio Rebecca Crane David Park	FOR THE PLAINTIFFS
Vincent de Grandpré Emily Kettel Benjamin Reingold Jasmine Godfrey Nyrie Israelian	FOR THE DEFENDANT

SOLICITORS OF RECORD:

BELMORE NEIDRAUER LLP Barristers and Solicitors Toronto, Ontario	FOR THE PLAINTIFFS
MARKWELL CLARIZIO LLP Barristers and Solicitors Toronto, Ontario	FOR THE PLAINTIFFS
BENNETT JONES LLP Barristers and Solicitors Toronto, Ontario	FOR THE DEFENDANT