Supplemental Material

Appendix I. Inclusion and Exclusion Criteria

I. Patient Inclusion Criteria

1. Male or female patients ≥18 years of age
2. Paroxysmal nocturnal hemoglobinuria (PNH) diagnosis confirmed by documented high-sensitivity flow cytometry (red blood cells [RBCs] and/or granulocytes)
3. Mean lactate dehydrogenase (LDH) ≥3 × upper limit of normal (ULN), based on 2 measurements from separate blood samples collected at least 1 day apart during screening
4. Willing and able to give written informed consent and comply with the study visit schedule
5. Documented meningococcal vaccination not more than 3 years prior to dosing
6. Female patients who consider themselves postmenopausal must provide evidence at screening of menopause status, based on a combination of amenorrhea for at least 1 year and increased serum follicle-stimulating hormone level (>30 IU/L) on at least 2 occasions (eg, in the absence of hormone replacement therapy, dietary phytoestrogens) or estradiol concentration <10 pg/mL
7. Female patients of childbearing potential must use highly effective contraception as defined below, starting at screening and continuing until at least 6 to 8 months after the last dose of ravulizumab. Highly effective contraceptive methods are as follows:
    a. Combined (estrogen and progestogen) hormonal contraception associated with inhibition of ovulation:
        - Oral
        - Intravaginal
        - Transdermal
    b. Progesterone-only hormonal contraception associated with inhibition of ovulation
        - Oral

- Injectable
- Implantable

c. Intrauterine device
d. Intrauterine hormone-releasing system
e. Bilateral tubal occlusion
f. Vasectomized partner, provided that the partner is the patient's sole sexual partner
g. Sexual abstinence, defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments; reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the subject
h. Combination of male condom with appropriate barrier methods for the female patient (double barrier methods)

8. Male patients with a female spouse/partner of childbearing potential or a pregnant or breastfeeding spouse or partner must agree to use barrier contraception (male condom) during the treatment period and for at least 6 to 8 months after the last dose of ravulizumab. Barrier contraception is required even with documented medical assessment of surgical success of a vasectomy. Female spouses/partners of male patients who are of childbearing potential must use highly effective contraception (as defined in inclusion criterion #7) or acceptable contraception, as defined below, starting at screening and continuing until at least 6 to 8 months after the last dose of ravulizumab. Male patients must not donate sperm during the screening and treatment periods and for at least 6 to 8 months after the last dose of ravulizumab.
    a. Acceptable contraceptive methods are as follows: simultaneous use of male condom and appropriate barrier methods for the female partner

II. Patient Exclusion Criteria

1. Treatment with a complement inhibitor at any time
2. Platelet count 30 × 10^9/L (<30,000/mm^3) at screening
3. Absolute neutrophil count 0.5 × 10^9/L (<500/μL) at screening

4. History of bone marrow transplantation
5. History of *Neisseria meningitidis* infection or history of unexplained, recurrent infection; or infection requiring treatment with systemic antibiotics within the last 90 days prior to dosing
6. Female patients who are planning to become pregnant, or are pregnant or breastfeeding
7. Positive pregnancy test at screening or day 1
8. Patients are excluded if they are taking any of the following medications and are not on a stable regimen (as judged by the Investigator) for the time period indicated prior to screening:
    a. Erythropoietin or immunosuppressants for at least 8 weeks
    b. Corticosteroids for at least 4 weeks
    c. Vitamin K antagonists (eg, warfarin) with a stable international normalized ratio (per Investigator discretion) for at least 4 weeks
    d. Iron supplements or folic acid for at least 4 weeks
    e. Low molecular weight heparin for at least 4 weeks
9. Unexplained alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >ULN of the testing laboratory at screening (Study 103 only)
10. Human immunodeficiency virus (HIV) infection (evidenced by HIV-1 or HIV-2 antibody titer)
11. Acute or chronic hepatitis B virus infection (evidenced by the presence of hepatitis B surface antigen or immunoglobulin M antibodies against hepatitis B core antigen)
12. Acute or chronic hepatitis C virus infection (evidenced by hepatitis C virus antibody)
13. Active systemic bacterial, viral, or fungal infection within 14 days prior to dosing on day 1
14. Immunization with a live-attenuated vaccine 1 month prior to dosing on day 1
15. Participation in an interventional clinical study within 30 days before initiation of dosing on day 1, or use of any experimental therapy within 30 days prior to dosing on day 1, or within 5 half-lives of the investigational product, whichever is greater

16. Major surgery within 90 days prior to dosing on day 1
17. Presence of fever ≥38°C within 2 weeks prior to the first dosing on day 1
18. Patients with a history of malignancy within 5 years of screening with the exception of a nonmelanoma skin cancer or carcinoma in situ of the cervix that has been treated with no evidence of recurrence
19. Known history of severe allergic or anaphylactic reactions to any drug (including vaccines) or allergen
20. History of allergy to excipients of ravulizumab (eg, polysorbate 80)
21. Known allergy to Chinese hamster ovary cell proteins
22. History of any clinically significant cardiac, hepatic, immunologic, pulmonary, or rheumatoid disease that, in the Investigator's judgment, would preclude participation
23. Inability to comply with study requirements
24. Other unspecified reasons that, in the opinion of the Investigator or Sponsor, make the patient unsuitable for enrollment

Appendix II: Patient Narratives

A. Aplastic Anemia

A 49-year-old female enrolled in cohort 1 of Study 201 had low platelet and neutrophil counts (history of pancytopenia) at screening. She developed fever and neutropenia on day 99 of treatment, which required platelet and packed RBC transfusion. Based on bone marrow biopsy and confirmatory diagnosis of moderate aplastic anemia, the patient was started on cyclosporine.

B. RBC/Platelet Transfusions

Bone marrow insufficiency coexists to a varying extent in many patients with PNH, even without the formal diagnosis of aplastic anemia or myelodysplastic syndrome (MDS). Of the 6 patients who continued to require RBC/platelet transfusion in the 2 studies, 3 had a medical history of aplastic anemia or MDS. In these 3 patients, the continued need for transfusions was likely due to the consequences of severe underlying bone marrow insufficiency and not intravascular hemolysis—the 2 principal and independent pathologic processes requiring transfusions. For the 3 patients who did not have a formal diagnosis of aplastic anemia or MDS, 1 patient received a transfusion on day 1 only; the other 2 patients had suppressed intravascular hemolysis, as evidenced by normal range LDH levels, and presumably required transfusions on treatment due to underlying bone marrow dysfunction.[1] Overall, the results of our study are similar to those reported by Hillmen et al,[2] who found that 51% of transfusion-dependent patients became transfusion-independent following eculizumab treatment.

C**. Meningococcal Infections**

A 28-year-old male enrolled in cohort 2 had a prior medical history including renal insufficiency and a granuloma on his hand. He was diagnosed with PNH approximately 3 years prior to study entry. The patient received meningococcal ACWY and B vaccines 23 days prior to initiating ravulizumab and was also receiving penicillin prophylaxis. On study day 56, the patient was admitted to the hospital with a 12-hour history of malaise, muscle pain, and fever, and was initially diagnosed as having a viral infection. He was started on intravenous (IV) ceftriaxone and was transferred to the intensive care unit due to septic/cardiogenic shock and myocarditis. Culture results were positive for *N. meningitidis*, serotype Y/W135; the meningococcal isolate was found to be intermediate in sensitivity to penicillin. The patient was treated for the meningococcal infection, recovered, and was discharged from the hospital; he is continuing in the study.

An 18-year-old male enrolled in cohort 3 was diagnosed with PNH 2 months prior to study entry and received meningococcal ACWY and B vaccines on 44 and 15 days, respectively, prior to initiating ravulizumab; he was not receiving penicillin prophylaxis. On study day 221, the patient started experiencing vomiting, and was hospitalized the same day with symptoms of vomiting, malaise, confusion/delirium, worsening of general health conditions, and petechial rash and purpura on his arms, legs, and feet. He was started on IV ceftriaxone 4 g, which was subsequently changed to 2 g every 12 hours. The patient was subsequently transferred to an intensive care unit. A dose of ravulizumab 2400 mg was administered for breakthrough hemolysis (LDH level was 507 U/L). Culture results were positive for *N. meningitidis*, serotype Y. The patient improved, the ceftriaxone was

discontinued, and he was discharged from the hospital with a small lesion/necrosis/hematoma on his right heel that was almost healed at the time of discharge. The patient is continuing in the study.

References

1. Risitano AM, Rotoli B. Paroxysmal nocturnal hemoglobinuria: pathophysiology, natural history and treatment options in the era of biological agents. *Biologics*. 2008;2(2):205-222.
2. Hillmen P, Young NS, Schubert J, et al. The complement inhibitor eculizumab in paroxysmal nocturnal hemoglobinuria. *N Engl J Med*. 2006;355(12):1233-1243.

Appendix III. Listing of Study Investigators

Study 103: Jong Wook Lee, The Catholic University of Korea, Seoul St. Mary's Hospital, Seoul, Republic of Korea; Je-Hwan Lee, Asan Medical Center, Seoul, Republic of Korea; Jun Ho Jang, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; Jin Seok Kim, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; Sung-Soo Yoon, Seoul National University Hospital, Seoul, Republic of Korea; Hawk Kim, Ulsan University Hospital, Ulsan, Republic of South Korea; Anthony Mills, Princess Alexandra Hospital, Woolloongabba, Australia; Danny Hsu, Liverpool Hospital, Liverpool, Australia; Jeffrey Szer, Royal Melbourne Hospital, Melbourne, Australia.

Study 201: Alexander Röth, University Hospital Essen, Essen, Germany; Jong Wook Lee, The Catholic University of Korea, Seoul St. Mary's Hospital, Seoul, Republic of Korea; Louis Terriou, Hôpital Claude Huriez – CHU, Lille, France; Hubert Schrezenmeier, Universitaetslinikum, Ulm, Germany; Anita Hill, St. James's University Hospital, Leeds, UK; Alvaro Urbano, Hospital Clinic de Barcelona, Barcelona, Spain; Richard A. Wells, Sunnybrook Health Sciences Centre, Toronto, Canada; Jin Seok Kim, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; F. Ataulfo Gonzalez-Fernandez, Hospital Clinico San Carlos, Madrid, Spain; Fiorenza Barraco, Centre Hospitalier, Lyon-Sud, France; Austin G. Kulasekararaj, King's College Hospital, London, UK; Sung-Soo Yoon, Seoul National University Hospital, Seoul, Republic of Korea; Hsin-An Hou, National Taiwan University Hospital, Taipei City, Taiwan; Jens Panse, Universitaetsklinikum, Aachen, Germany; Lindsay Mitchell, Monklands Hospital, Airdrie, UK.

Supplemental Tables

Table S1. Change in Free Hemoglobin, Haptoglobin, and Reticulocytes

	Study 201				Study 103	
	Cohort 1 1000 mg q4w n=6	**Cohort 2 1600 mg q6w n=6**	**Cohort 3 2400 mg q8w n=7**	**Cohort 4 5400 mg q12w n=7**	**Cohort 1 900 mg q4w n=6**	**Cohort 2 1800 mg q4w n=7**
Free Hemoglobin[*]						
Baseline, mean (SD), mg/L	273.0 (172.29)	234.5 (109.65)	371.0 (278.16)	507.0 (288.97)	237.2 (83.43)	264.4 (109.05)
Endpoint,[†] mean (SD), mg/L	382.3 (654.27)	205.2 (139.28)	193.4 (153.80)	250.6 (91.87)[‡]	168.0 (79.48)	144.0 (62.98)
Percent change from baseline, mean (SD)	14.07 (124.755)	-10.00 (55.812)	-22.14 (94.388)	-34.74 (26.534)[‡]	-22.34 (42.225)	-43.97 (24.767)
Total Hemoglobin[§]						
Baseline, mean (SD), g/L	109.5 (19.74)	100.2 (20.93)[‡]	95.9 (20.07)	90.9 (11.73)	97.3 (11.91)	92.0 (21.42)
Endpoint,[‖] mean (SD), g/L	119.5 (12.63)	113.4 (19.93)[‡]	105.1 (21.11)	109.1 (18.88)	115.5 (12.37)	101.0 (14.01)
Change from baseline, mean (SD)	10.0 (14.75)	13.2 (11.48)[‡]	9.3 (19.15)	18.3 (17.76)	18.2 (10.46)	9.0 (12.68)
Haptoglobin[¶]						
Baseline, mean, g/L	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10
Endpoint,[†] mean (SD), g/L	0.122 (0.0531)	0.182 (0.2000)	0.104 (0.0113)	0.107 (0.0163)[#]	0.140 (0.0551)	0.117 (0.0454)
Percent change from baseline, mean (SD)	21.67 (53.072)	81.67 (200.042)	4.29 (11.339)	6.67 (16.33)[#]	40.00 (55.136)	17.14 (45.356)
Reticulocytes[**]						

Baseline, mean (SD), 10^{12}/L	0.1508 (0.06227)	0.1640 (0.06675)[‡]	0.2182 (0.04158)	0.2252 (0.06230)[#]	0.2043 (0.06592)[††]	0.1549 (0.05066)
Endpoint,[†] mean (SD), 10^{12}/L	0.1470 (0.06011)	0.1766 (0.10258)[‡]	0.2257 (0.06992)[#]	0.2148 (0.08117)[#]	0.1633 (0.07130)[††]	0.2031 (0.10671)
Change from baseline, mean (SD)	-0.0038 (0.05258)	0.0126 (0.05807)[‡]	0.0075 (0.09647)[#]	-0.0103 (0.10157)[#]	-0.0410 (0.02197)[††]	0.0483 (0.09403)

Abbreviations: q4w, every 4 weeks; q6w, every 6 weeks; q8w, every 8 weeks; q12w, every 12 weeks; SD, standard deviation.

[*]Reference range for free hemoglobin, 0–152 mg/L

[†]Study 103: day 169; Study 201, Cohorts 1–3: day 253; Study 201, Cohort 4: day 281.

[‡]n=5.

[§]Reference range for total hemoglobin, men: 127-181 g/L, women: 116-164 g/L.

[‖]Study 103: day 169; Study 201, day 253.

[¶]Reference range for haptoglobin, 0.3–2.0 g/L; lower limit of detection, 0.1 g/L.

[#]n=6.

[**]Reference range for reticulocytes, 0.03–0.13 x 10^{12}/L.

[††]n=4.

Table S2. EORTC QLQ-C30 Functional Scales

		Study 201				Study 103	
Scale	**Measure**	**Cohort 1 1000 mg q4w n=6**	**Cohort 2 1600 mg q6w n=6**	**Cohort 3 2400 mg q8w n=7**	**Cohort 4 5400 mg q12w n=7**	**Cohort 1 900 mg q4w n=6**	**Cohort 2 1800 mg q4w n=7**
Global Health Status/QoL	Baseline, mean (SD)	50.0 (24.30)*	50.0 (14.91)	51.2 (21.74)	46.4 (21.44)	54.2 (20.92)	44.0 (20.81)
	Endpoint†, mean (SD)	62.5 (10.21)	63.3 (18.26)*	76.4 (21.99)‡	68.1 (21.35)‡	77.8 (13.61)	71.4 (18.54)
	Change from baseline, mean (SD)	8.3 (29.34)	16.7 (11.79)*	27.8 (27.72)‡	27.8 (27.21)‡	23.6 (23.81)	27.4 (23.92)
Physical Functioning	Baseline, mean (SD)	73.3 (14.14)*	71.1 (28.49)	76.2 (19.19)	76.2 (21.72)	72.2 (17.08)	59.0 (26.23)
	Endpoint†, mean (SD)	88.9 (6.88)	77.3 (22.90)*	93.3 (8.43)‡	86.7 (8.43)‡	87.8 (14.25)	82.9 (11.45)
	Change from baseline, mean (SD)	11.1 (13.11)	12.0 (9.89)*	20.0 (16.33)‡	11.1 (18.70)‡	15.6 (9.11)	23.8 (23.37)
Role Functioning	Baseline, mean (SD)	76.7 (22.36)*	55.6 (40.37)	61.9 (26.72)	66.7 (19.24)	61.1 (22.77)	64.3 (27.94)
	Endpoint†, mean (SD)	77.8 (17.21)	66.7 (31.18)*	80.6 (26.70)‡	77.8 (13.61)‡	88.9 (17.21)	88.1 (15.85)
	Change from baseline, mean (SD)	2.8 (34.02)	20.0 (32.06)*	22.2 (36.00)‡	13.9 (16.39)‡	27.8 (8.61)	23.8 (23.29)
Emotional Functioning	Baseline, mean (SD)	65.0 (37.92)	66.7 (32.91)	65.5 (29.44)	75.0 (14.43)	66.7 (17.48)	58.3 (26.35)
	Endpoint†, mean (SD)	66.7	81.7	87.5	87.5	88.9	77.4

		(13.94)	(19.00)*	(16.46)‡	(16.46)‡	(17.21)	(27.52)
	Change from baseline, mean (SD)	6.9 (24.39)	18.3 (19.90)*	26.4 (35.52)‡	15.3 (22.62)‡	22.2 (16.39)	19.0 (13.36)
Cognitive Functioning	Baseline, mean (SD)	63.3 (44.72)*	77.8 (29.19)	78.6 (20.89)	85.7 (17.82)	75.0 (31.18)	52.4 (24.40)
	Endpoint†, mean (SD)	75.0 (17.48)	73.3 (34.56)*	94.4 (8.61)‡	86.1 (16.39)‡	80.6 (22.15)	81.0 (17.82)
	Change from baseline, mean (SD)	8.3 (29.34)	0 (11.78)*	13.9 (19.48)‡	2.8 (16.39)‡	5.6 (31.03)	28.6 (12.60)
Social Functioning	Baseline, mean (SD)	60.0 (40.14*	52.8 (42.71)	69.0 (33.92)	83.3 (25.46)	63.9 (34.02)	61.9 (24.93)
	Endpoint†, mean (SD)	83.3 (14.91)	66.7 (31.18)*	86.1 (16.39)‡	86.1 (16.39)‡	86.1 (16.39)	76.2 (26.97)
	Change from baseline, mean (SD)	22.2 (41.72)	16.7 (28.87)*	19.4 (37.14)‡	5.6 (31.03)‡	22.2 (25.09)	14.3 (29.55)

Each subscale has a range of 0 to 100, with a high score representing a higher response level. A high score for a functional scale represents a high level of functioning; a high score for a symptom scale represents a high level of symptomatology.

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; q4w, every 4 weeks; q6w, every 6 weeks; q8w, every 8 weeks; q12w, every 12 weeks; SD, standard deviation.

*n=5.

†Study 103: day 169 Study 201, Cohorts 1–3: day 253; Study 201, Cohort 4: day 281.

‡n=6.

Table S3. EORTC QLQ-C30 Symptom Scales

		Study 201				Study 103	
Scale	**Measure**	**Cohort 1 1000 mg q4w n=6**	**Cohort 2 1600 mg q6w n=6**	**Cohort 3 2400 mg q8w n=7**	**Cohort 4 5400 mg q12w n=7**	**Cohort 1 900 mg q4w n=6**	**Cohort 2 1800 mg q4w n=7**
Fatigue	Baseline, mean (SD)	42.2 (27.67)*	51.9 (30.36)	49.2 (33.86)	41.3 (28.48)	53.7 (14.77)	57.1 (28.28)
	Endpoint,† mean (SD)	25.9 (11.47)	33.3 (39.28)*	25.9 (25.98)‡	22.2 (14.05)‡	22.2 (21.08)	34.9 (21.69)
	Change from baseline, mean (SD)	–14.8 (30.36)	–26.7 (16.85)*	–25.9 (32.71)‡	-22.2 (25.34)‡	-31.5 (16.36)	-22.2 (18.15)
Nausea and vomiting	Baseline, mean (SD)	3.3 (7.46)*	2.8 (6.81)	14.3 (24.40)	4.8 (12.60)	11.1 (13.61)	23.8 (28.64)
	Endpoint,† mean (SD)	0.0 (0.0)	0.0 (0.0)*	0.0 (0.0)‡	5.6 (8.61)‡	2.8 (6.81)	2.4 (6.30)
	Change from baseline, mean (SD)	–2.8 (6.81)	–3.3 (7.46)*	–16.7 (25.82)‡	0 (10.54)‡	-8.3 (9.13)	-21.4 (29.99)
Pain	Baseline, mean (SD)	6.7 (14.91)*	8.3 (13.94)	23.8 (30.21)	9.5 (16.26)	22.2 (25.09)	35.7 (27.93)
	Endpoint,† mean (SD)	11.1 (27.22)	0.0 (0.0)*	13.9 (26.70)‡	11.1 (13.61)‡	0.0 (0.0)	16.7 (23.57)
	Change from baseline, mean (SD)	2.8 (34.02)	–10.0 (14.91)*	–13.9 (38.61)‡	0 (10.54)‡	-22.2 (25.09)	-19.0 (22.42)
Dyspnea	Baseline, mean (SD)	26.7 (14.91)*	55.6 (34.43)	33.3 (38.49)	33.3 (27.22)	38.9 (25.09)	52.4 (32.53)
	Endpoint,† mean (SD)	16.7 (18.26)	33.3 (33.34)*	11.1 (17.21)‡	11.1 (17.21)‡	11.1 (17.21)	19.0 (17.82)
	Change from baseline,	–11.1	–33.3	–27.8	-16.7	-27.8	-33.3

	mean (SD)	(17.21)	(23.57)*	(44.31)‡	(18.26)‡	(25.09)	(27.22)
Insomnia	Baseline, mean (SD)	20.0 (18.26)*	16.7 (18.26)	38.1 (40.50)	23.8 (25.20)	22.2 (17.21)	61.9 (35.64)
	Endpoint,† mean (SD)	22.2 (34.43)	13.3 (18.26)*	16.7 (18.26)‡	16.7 (18.26)‡	16.7 (18.26)	42.9 (31.71)
	Change from baseline, mean (SD)	5.6 (25.09)	0 (23.57)*	-22.2 (45.54)‡	-11.1 (27.22)‡	-5.6 (25.09)	-19.0 (17.82)
Appetite loss	Baseline, mean (SD)	13.3 (18.26)*	16.7 (27.89)	19.0 (26.23)	19.0 (17.82)	16.7 (18.26)	38.1 (35.64)
	Endpoint,† mean (SD)	0.0 (0.0)	0.0 (0.0)*	5.6 (13.61)‡	11.1 (17.21)‡	5.6 (13.61)	23.8 (25.20)
	Change from baseline, mean (SD)	–11.1 (17.21)	–20.0 (29.82)*	–16.7 (34.96)‡	–11.1 (17.21)‡	-11.1 (17.21)	-14.3 (26.23)
Constipation	Baseline	13.3 (18.26)*	20.0 (44.72)*	28.6 (35.64)	14.3 (26.23)	33.3 (36.51)	23.8 (16.26)
	Endpoint,† mean (SD)	5.6 (13.61)	0.0 (0.0)*	11.1 (17.21)‡	5.6 (13.61)‡	22.2 (40.37)	14.3 (17.82)
	Change from baseline, mean (SD)	–5.6 (13.61)	–25.0 (50.00)§	–22.2 (40.37)‡	–11.1 (17.21)‡	-11.1 (27.21)	-9.5 (25.20)
Diarrhea	Baseline, mean (SD)	6.7 (14.91)*	11.1 (27.22)	9.5 (16.26)	4.8 (12.60)	5.6 (13.61)	9.5 (16.26)
	Endpoint,† mean (SD)	0.0 (0.0)	6.7 (14.91)*	5.6 (13.61)‡	0.0 (0.0)‡	0.0 (0.0)	4.8 (12.60)
	Change from baseline, mean (SD)	–11.1 (17.21)	–6.7 (36.52)*	–5.6 (25.09)‡	-5.6 (13.61)‡	-5.6 (13.61)	-4.8 (23.00)
Financial difficulties	Baseline, mean (SD)	26.7 (43.46)*	27.8 (38.97)	19.0 (37.80)	23.8 (25.20)	33.3 (42.16)	42.9 (37.09)
	Endpoint,† mean (SD)	27.8	26.7	5.6	11.1	11.1	14.3

		(32.77)	(43.46)*	(13.61)‡	(17.21)‡	(17.21)	(26.23)
	Change from baseline, mean (SD)	5.6 (32.77)	0.0 (0.0)*	–16.7 (40.82)‡	-11.1 (17.21)‡	-22.2 (27.22)	-28.6 (29.99)

Each subscale has a range of 0 to 100, with a high score representing a higher response level. A high score for a functional scale represents a high level of functioning; a high score for a symptom scale represents a high level of symptomatology.

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; q4w, every 4 weeks; q6w, every 6 weeks; q8w, every 8 weeks; q12w, every 12 weeks; SD, standard deviation.

*n=5.

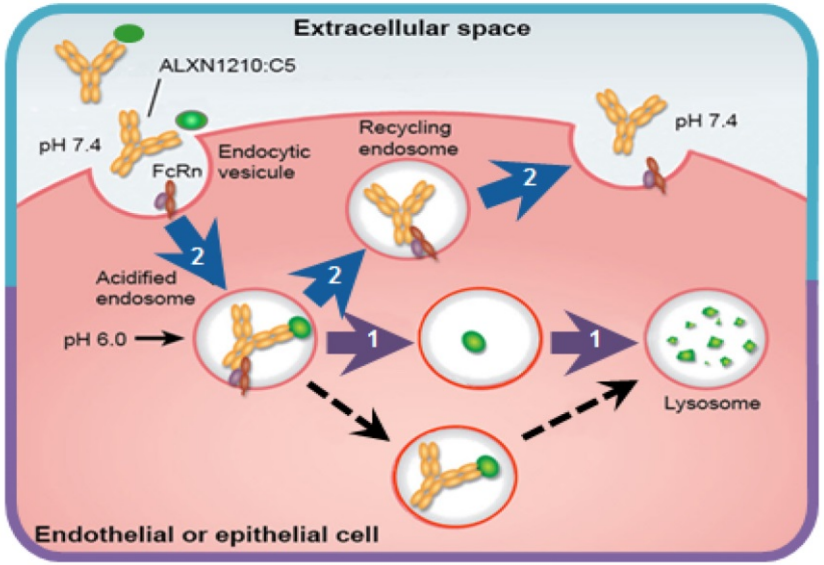
†Study 103: day 169; Study 201, Cohorts 1–3: day 253; Study 201, Cohort 4: day 281.

‡n=6.

§n=4.

Supplemental Figures

Figure S1. Ravulizumab (ALXN1210): mechanism of extended duration of action.[1] FcRn, neonatal Fc receptor. Image courtesy of Alexion Pharmaceuticals, Inc.



1	pH-Dependent Release of C5	As endosomal pH falls below 6.0, the affinity of ravulizumab for C5 weakens, favoring their dissociation, hence minimizing target-mediated drug disposition
2	Enhanced FcRn Recycling	At lower endosomal pH, the affinity of ravulizumab for FcRn strengthens, increasing the probability of free ALXN1210 recycling back to circulation

Target-Mediated Drug Disposition

1. Sheridan D, Yu ZX, Zhang Y, et al. Design and preclinical characterization of ALXN1210: a novel anti-C5 antibody with extended duration of action. *PLoS One.* 2018;13(3):e0195909.

Figure S2. Distribution of patients from screening through maintenance period. LDH, lactate dehydrogenase.