

## **Data Supplement**

### **A Phase 1 Randomized, Double-Blind, Placebo-Controlled, Cohort Dose-Escalation Study of a Human Monoclonal Antibody to IL-6 in Patients with CKD**

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**Supplemental Table 1.** Additional Clinical Parameters

Variable	Placebo (n=3)		Ziltivekimab 5 mg (n=3)		Ziltivekimab 15 mg (n=3)		Ziltivekimab 50 mg (n=3)		All Active Groups (n=9)	
	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12
<b>Chemistry:</b>										
<b>Alanine aminotransferase, U/L</b>	20.3 ± 7.6	28.0 ± 13.4	44.7 ± 45.3	51.0 ± 56.3	17.7 ± 7.8	20.0 ± 10.4	17.7 ± 1.5	25.3 ± 9.5	26.7 ± 26.7	32.1 ± 32.4
<b>Albumin, g/dL</b>	4.3 ± 0.0	4.4 ± 0.2	4.0 ± 0.2	3.9 ± 0.4	4.1 ± 0.1	4.3 ± 0.2	4.2 ± 0.1	4.5 ± 0.2	4.1 ± 0.1	4.2 ± 0.3
<b>Alkaline phosphatase, U/L</b>	67.0 ± 30.8	67.0 ± 36.4	79.0 ± 25.5	87.0 ± 41.0	83.3 ± 17.9	72.3 ± 17.9	67.0 ± 18.0	53.7 ± 9.5	76.4 ± 19.4	71.0 ± 27.0
<b>Anion gap, mmol/L</b>	11.7 ± 2.5	11.7 ± 2.3	9.3 ± 1.2	8.0 ± 1.7	9.0 ± 1.0	9.3 ± 1.5	11.0 ± 1.7	9.7 ± 1.2	9.8 ± 1.5	9.0 ± 1.5
<b>Aspartate aminotransferase, U/L</b>	20.0 ± 2.7	26.0 ± 7.6	29.0 ± 18.2	38.7 ± 29.8	17.7 ± 3.1	19.3 ± 4.9	16.7 ± 1.5	22.7 ± 5.1	1.1 ± 11.0	26.9 ± 17.8
<b>Bilirubin, mg/dL</b>	0.5 ± 0.2	0.5 ± 0.1	0.6 ± 0.2	0.6 ± 0.2	0.6 ± 0.2	0.5 ± 0.2	0.8 ± 0.1	0.8 ± 0.2	0.6 ± 0.2	0.6 ± 0.2
<b>Calcium, mg/dL</b>	9.7 ± 0.2	9.7 ± 0.2	9.6 ± 0.5	9.4 ± 0.7	9.6 ± 0.3	9.5 ± 0.4	9.3 ± 0.2	9.3 ± 0.4	9.5 ± 0.3	9.4 ± 0.5
<b>Carbon dioxide, mmol/L</b>	22.3 ± 2.5	23.0 ± 1.0	23.3 ± 4.9	22.7 ± 4.0	25.0 ± 1.0	24.3 ± 2.3	24.0 ± 1.7	25.3 ± 1.2	24.1 ± 2.8	24.1 ± 2.7
<b>Chloride, mmol/L</b>	103.3 ± 0.6	106.0 ± 2.0	105.7 ± 7.1	105.3 ± 6.5	108.3 ± 2.1	109.0 ± 4.0	107.0 ± 2.7	107.7 ± 2.5	107.0 ± 4.1	107.3 ± 4.3
<b>Direct bilirubin, mg/dL</b>	0.07 ± 0.06	0.10 ± 0.00	0.13 ± 0.06	0.10 ± 0.1	0.17 ± 0.06	0.13 ± 0.06	0.13 ± 0.06	0.17 ± 0.06	0.14 ± 0.05	0.13 ± 0.07
<b>Glucose, mg/dL</b>	168 ± 37	123 ± 30	116 ± 29	105 ± 18	130 ± 46	102 ± 10	131 ± 48	167 ± 65	126 ± 37	125 ± 47
<b>Indirect bilirubin, mg/dL</b>	0.4 ± 0.1	0.4 ± 0.1	0.5 ± 0.2	0.5 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	0.6 ± 0.1	0.7 ± 0.2	0.5 ± 0.2	0.5 ± 0.2
<b>Potassium, mmol/L</b>	3.8 ± 0.5	3.9 ± 0.5	4.2 ± 0.2	4.5 ± 0.2	3.9 ± 0.3	4.4 ± 0.4	3.9 ± 0.3	3.7 ± 0.4	4.0 ± 0.2	4.2 ± 0.5
<b>Protein, g/dL</b>	7.3 ± 0.1	7.5 ± 0.3	7.0 ± 0.1	7.1 ± 0.3	7.1 ± 0.1	7.0 ± 0.6	6.9 ± 0.4	6.9 ± 0.5	7.0 ± 0.2	7.0 ± 0.4

Variable	Placebo		Ziltivekimab 5 mg		Ziltivekimab 15 mg		Ziltivekimab 50 mg		All Active Groups (n=9)	
	(n=3)		(n=3)		(n=3)		(n=3)			
	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12
Sodium, g/dL	137 ± 2	141 ± 1	138 ± 4	136 ± 4	142 ± 2	143 ± 2	142 ± 2	143 ± 3	141 ± 3	140 ± 4
Urea nitrogen, mg/dL	53 ± 19	41 ± 11	35 ± 20	31 ± 12	29 ± 7	35 ± 10	30 ± 10	28 ± 7	31 ± 12	31 ± 9
<b>Hematology:</b>										
Basophils, 10 <sup>3</sup> / µL	0.07 ± 0.06	0.07 ± 0.06	0.03 ± 0.06	0.03 ± 0.06	0.13 ± 0.06	0.03 ± 0.06	0.03 ± 0.06	0.07 ± 0.06	0.07 ± 0.07	0.08 ± 0.07
Basophils / leukocytes, %	0.77 ± 0.55	0.87 ± 0.31	0.47 ± 0.25	0.53 ± 0.29	1.0 ± 0.62	1.07 ± 0.65	0.93 ± 0.61	0.97 ± 0.25	0.80 ± 0.52	0.66 ± 0.45
Eosinophils, 10 <sup>3</sup> / µL	0.17 ± 0.06	0.20 ± 0.10	0.27 ± 0.21	0.30 ± 0.17	0.37 ± 0.21	0.17 ± 0.25	0.20 ± 0.10	0.23 ± 0.15	0.28 ± 0.17	0.29 ± 0.18
Eosinophils / leukocytes, %	3.0 ± 1.4	3.3 ± 2.0	3.2 ± 2.7	3.8 ± 1.5	3.2 ± 1.8	3.1 ± 1.7	4.2 ± 2.6	4.7 ± 3.1	3.5 ± 1.8	3.9 ± 2.0
Mean corpuscular HGB Concentration, g/dL	32.8 ± 1.1	32.3 ± 1.3	33.7 ± 0.6	34.2 ± 0.7	33.2 ± 1.2	33.8 ± 1.7	34.0 ± 0.5	34.1 ± 0.4	33.6 ± 0.8	34.0 ± 0.9
Mean corpuscular HGB, pg	30.2 ± 2.0	29.7 ± 1.8	30.6 ± 1.9	31.3 ± 2.8	29.9 ± 2.1	30.6 ± 1.7	31.5 ± 0.2	32.2 ± 0.3	30.7 ± 1.6	31.3 ± 1.8
Mean corpuscular Volume, fL	91.8 ± 3.7	92.2 ± 2.7	91.1 ± 7.2	91.3 ± 6.7	90.4 ± 9.1	90.6 ± 7.3	92.8 ± 1.0	94.3 ± 1.7	91.4 ± 6.0	92.1 ± 5.3
Erythrocytes, 10 <sup>6</sup> / µL	4.3 ± 0.2	4.4 ± 0.3	4.5 ± 0.9	4.7 ± 0.6	4.7 ± 0.6	4.6 ± 0.5	4.9 ± 0.4	5.0 ± 0.2	4.7 ± 0.6	4.8 ± 0.4
Erythrocytes distribution width, %	14.3 ± 0.6	14.0 ± 0.8	13.4 ± 0.5	13.2 ± 0.4	14.1 ± 1.1	14.2 ± 0.9	13.3 ± 0.3	12.9 ± 0.4	13.6 ± 0.7	13.4 ± 0.8
Ferritin, ng/mL	104 (73, 213)	82 (29, 161)	41 (32, 74)	43 (17, 91)	92 (52, 135)	86 (56, 128)	270 (162, 327)	179 (118, 247)	137 (53, 162)	91 (56, 128)
Hematocrit, %	39.9 ± 3.7	40.8 ± 3.5	40.5 ± 6.1	42.6 ± 3.4	42.8 ± 6.6	41.7 ± 3.3	45.4 ± 3.0	47.5 ± 1.9	42.9 ± 5.2	44.9 ± 3.7
Hemoglobin, g/dL	13.1 ± 1.5	13.2 ± 1.3	13.7 ± 2.8	14.6 ± 1.3	14.2 ± 2.3	14.1 ± 1.7	15.4 ± 1.2	16.2 ± 0.8	14.4 ± 1.9	15.0 ± 1.5
Immature granulocytes, 10 <sup>9</sup> / L	0.03 ± 0.06	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.03 ± 0.06	0.1 ± 0.0	0.03 ± 0.06	0.0 ± 0.0	0.02 ± 0.04	0.03 ± 0.05

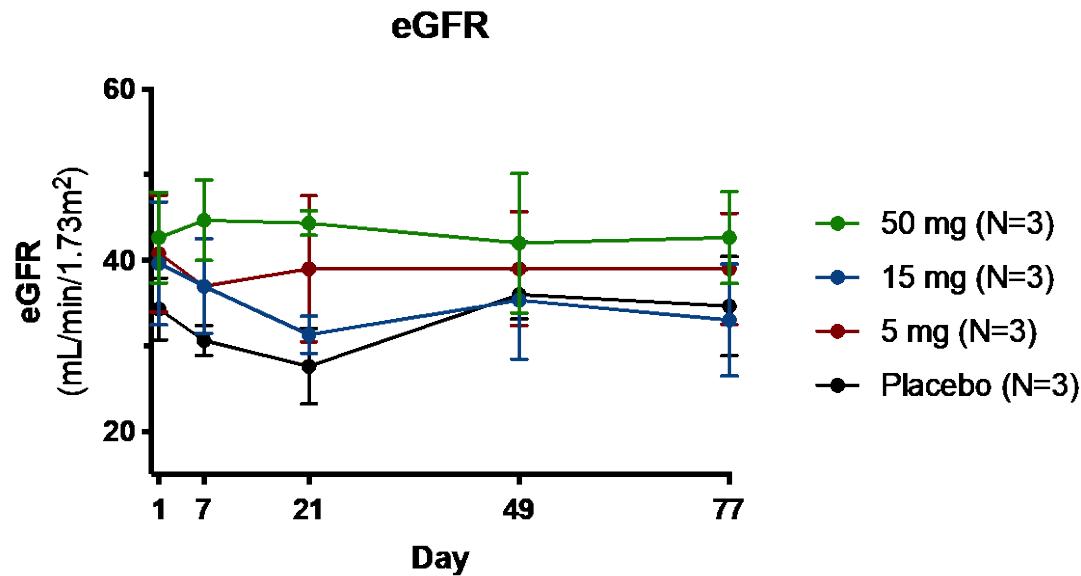
Variable	Placebo		Ziltivekimab 5 mg		Ziltivekimab 15 mg		Ziltivekimab 50 mg		All Active Groups (n=9)	
	(n=3)		(n=3)		(n=3)		(n=3)			
	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12
<b>Immature granulocytes / leukocytes, %</b>	0.4 ± 0.3	0.4 ± 0.2	0.3 ± 0.0	0.3 ± 0.2	0.6 ± 0.5	0.40 ± 0.3	0.6 ± 0.3	0.5 ± 0.3	0.5 ± 0.3	0.6 ± 0.2
<b>Immature reticulocyte fraction, %</b>	12.6 ± 4.6	12.1 ± 0.9	10.5 ± 3.6	13.6 ± 8.1	10.4 ± 3.6	7.2 ± 3.7	12.8 ± 3.6	11.0 ± 31.5	11.2 ± 3.4	10.6 ± 5.3
<b>Iron, µg/dL</b>	77 ± 11	75 ± 12	75 ± 17	83 ± 11	98 ± 9	109 ± 33	99 ± 31	99 ± 25	91 ± 20	97 ± 25
<b>Leukocytes, 10³ / µL</b>	6.2 ± 1.8	6.1 ± 1.2	7.9 ± 3.5	6.5 ± 2.3	10.7 ± 0.9	11.0 ± 1.7	5.0 ± 0.4	5.1 ± 0.8	7.9 ± 3.1	7.6 ± 3.0
<b>Lymphocytes, 10³ / µL</b>	1.7 ± 0.3	1.4 ± 0.2	1.5 ± 0.4	1.5 ± 0.5	1.7 ± 0.5	1.8 ± 0.2	1.2 ± 0.4	1.2 ± 0.3	1.5 ± 0.4	1.5 ± 0.4
<b>Lymphocytes / leukocytes, %</b>	27.6 ± 3.3	23.9 ± 5.8	21.2 ± 6.1	23.0 ± 4.6	16.3 ± 4.5	16.8 ± 3.4	24.4 ± 8.6	24.0 ± 8.6	20.6 ± 6.9	21.3 ± 6.3
<b>Monocytes, 10³ / µL</b>	0.5 ± 0.1	0.5 ± 0.1	0.6 ± 0.2	0.7 ± 0.3	0.8 ± 0.3	0.8 ± 0.2	0.4 ± 0.2	0.5 ± 0.2	0.6 ± 0.2	0.7 ± 0.2
<b>Monocytes / leukocytes, %</b>	8.4 ± 1.3	7.8 ± 2.2	8.4 ± 1.5	9.4 ± 1.3	7.3 ± 3.4	7.7 ± 2.0	9.4 ± 3.8	9.5 ± 3.5	8.4 ± 2.8	8.9 ± 2.3
<b>Neutrophils, 10³ / µL</b>	3.8 ± 1.5	4.0 ± 1.4	5.4 ± 2.8	4.3 ± 1.5	7.7 ± 1.4	7.9 ± 1.8	3.0 ± 0.9	3.1 ± 1.2	5.4 ± 2.6	5.1 ± 2.5
	59.8 ± 6.7	63.8 ± 10.2	66.4 ± 3.4	62.9 ± 6.7	71.6 ± 6.4	70.7 ± 5.0	60.4 ± 14.1	60.3 ± 14.2	66.1 ± 9.9	64.7 ± 9.0
<b>Nucleated erythrocytes, 10⁹ / L</b>	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.00 ± 0.01	0.0 ± 0.0	0.0 ± 0.0
<b>Platelets, 10³ / µL</b>	243 ± 101	263 ± 102	215 ± 59	212 ± 50	245 ± 30	242 ± 39	164 ± 45	146 ± 44	208 ± 53	200 ± 57
<b>Ret hemoglobin distribution width, pg</b>	34.1 ± 1.7	34.0 ± 1.8	34.7 ± 2.3	35.6 ± 2.5	34.7 ± 1.1	34.6 ± 2.1	37.2 ± 1.0	37.4 ± 0.8	35.6 ± 1.9	35.9 ± 2.1
<b>Reticulocytes, 10¹² / L</b>	0.06 ± 0.02	0.06 ± 0.01	0.08 ± 0.02	0.08 ± 0.03	0.06 ± 0.03	0.05 ± 0.01	0.10 ± 0.03	0.10 ± 0.01	0.08 ± 0.03	0.08 ± 0.03
<b>Reticulocytes / leukocytes, %</b>	1.4 ± 0.4	1.4 ± 0.2	1.8 ± 0.7	1.8 ± 0.4	1.3 ± 0.3	1.1 ± 0.2	2.2 ± 0.7	2.0 ± 0.2	1.7 ± 0.6	1.6 ± 0.5



Variable	Placebo (n=3)		Ziltivekimab 5 mg (n=3)		Ziltivekimab 15 mg (n=3)		Ziltivekimab 50 mg (n=3)		All Active Groups (n=9)	
	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12
<b>Urine Laboratory Tests:</b>										
<b>Spot urine creatinine, mg/dL</b>	60 ± 34	56 ± 9	80 ± 76	45 ± 39	133 ± 32	116 ± 71	150 ± 33	110 ± 77	118 ± 56	90 ± 66
<b>Spot urine protein, mg/dL</b>	20 (18, 20)	17 (9, 81)	41 (11, 133)	42 (5, 96)	11 (10, 28)	9 (8, 23)	14 (9, 19)	11 (7, 18)	15 (11, 35)	11 (8, 23)
<b>Urine protein:creatinine, ratio</b>	0.25 (0.23, 0.95)	0.30 (0.19, 1.25)	0.80 (0.39, 0.89)	1.07 (0.28, 1.62)	0.11 (0.07, 0.18)	0.12 (0.09, 0.15)	0.07 (0.07, 0.11)	0.09 (0.08, 0.25)	0.11 (0.07, 0.39)	0.15 (0.09, 0.28)
<b>Vital Signs:</b>										
<b>Body mass index, kg/m<sup>2</sup></b>	30.8 ± 2.2	30.9 ± 2.4	33.0 ± 5.2	33.2 ± 5.5	31.1 ± 4.9	31.0 ± 4.7	31.2 ± 7.9	31.1 ± 8.6	31.7 ± 5.4	31.8 ± 5.7
<b>Systolic blood pressure, mmHg</b>	140 ± 37	148 ± 12	127 ± 16	129 ± 10	146 ± 9	141 ± 8	130 ± 17	149 ± 21	134 ± 15	140 ± 15
<b>Diastolic blood pressure, mmHg</b>	72 ± 6	80 ± 10	74 ± 5	70 ± 8	72 ± 15	68 ± 10	72 ± 18	77 ± 2	73 ± 12	72 ± 7
<b>Heart rate, bpm</b>	62 ± 10	67 ± 14	60 ± 4	60 ± 8	69 ± 15	63 ± 13	61 ± 14	55 ± 8	63 ± 11	60 ± 9
<b>Respiration rate, breaths/min</b>	16 ± 4	16 ± 0	17 ± 2	17 ± 2	16 ± 0	17 ± 2	16 ± 0	19 ± 6	16 ± 1	18 ± 3
<b>Temperature, C</b>	36.0 ± 0.4	35.9 ± 1.0	36.2 ± 0.3	35.9 ± 0.4	36.7 ± 0.7	36.6 ± 0.5	35.7 ± 0.4	36.1 ± 0.8	36.2 ± 0.6	36.2 ± 0.6
<b>Weight, kg</b>	88 ± 13	88 ± 14	88 ± 24	89 ± 25	92 ± 20	91 ± 20	105 ± 33	105 ± 36	95 ± 24	95 ± 25

Data are mean±S.D.or median (IQR). HGB, hemoglobin.

**Supplemental Figure 1. Change in eGFR in response to Ziltivekimab.** Absolute change in estimated glomerular filtration rate (eGFR; ml/min/1.73m<sup>2</sup>) in response to Ziltivekimab treatment.



**Supplemental Figure 2. Change in albumin in response to Ziltivekimab.** Absolute concentrations of albumin (g/dL; Panel A) and change in albumin from baseline (Panel B) in response to Ziltivekimab treatment.

