Supporting information for:

Dupilumab Safety and Efficacy up to 1 Year in Children Aged 6 Months to 5 Years with Atopic Dermatitis: Results from a Phase 3 Open-Label Extension Study

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Supplementary figures

Fig. S1 Efficacy outcomes from PSBL through week 52 of the PED-OLE by patient baseline weight at OLE baseline.

(a) Proportion of patients achieving IGA 0/1, (b) Proportion of patients achieving EASI-75, (c) Mean % change (± SD) in EASI from PSBL

BL baseline of PED-OLE, *EASI* Eczema Area and Severity Index, *EASI-75* patients achieving a 75% reduction in EASI compared with PSBL, *IGA* Investigator's Global Assessment, *OLE* open-label extension, *PSBL* parent study baseline, *SD* standard deviation

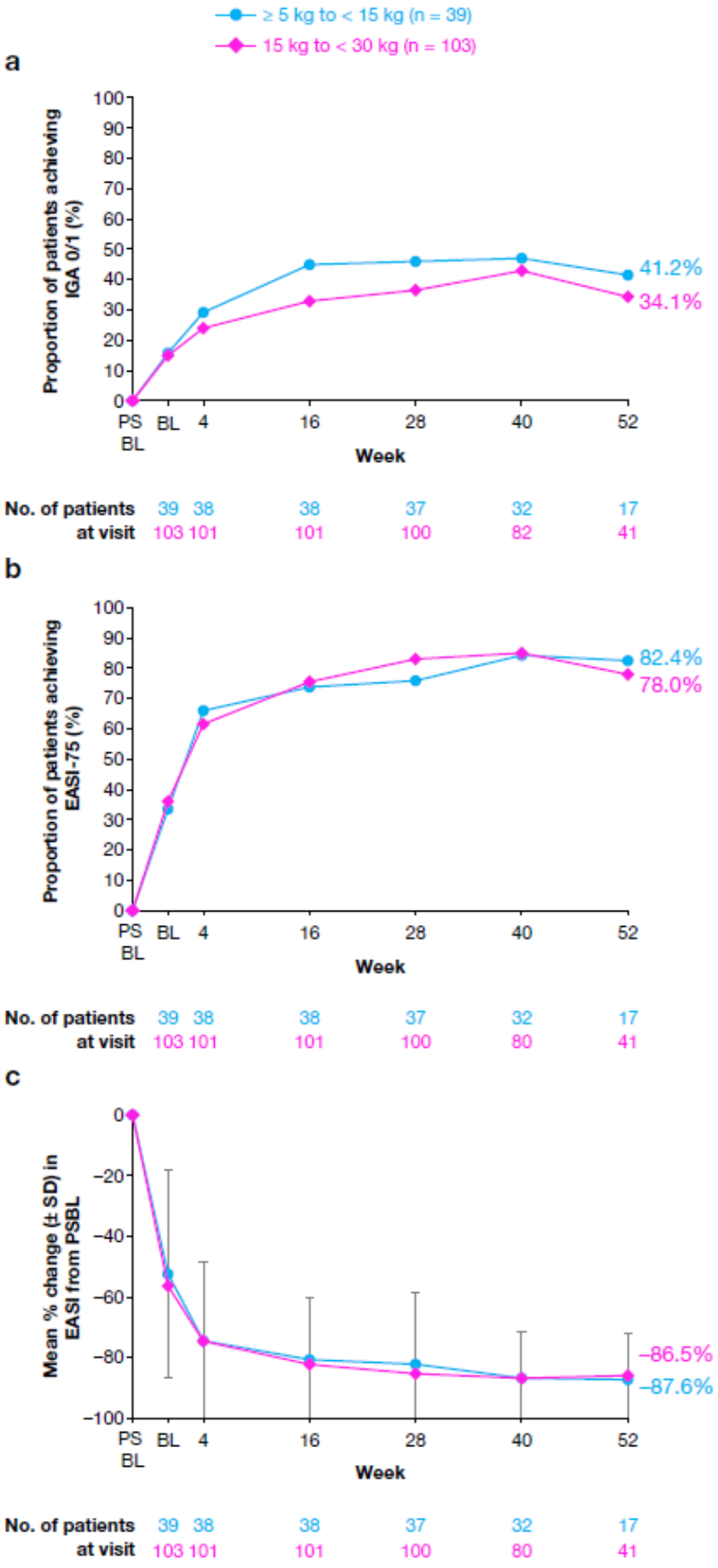
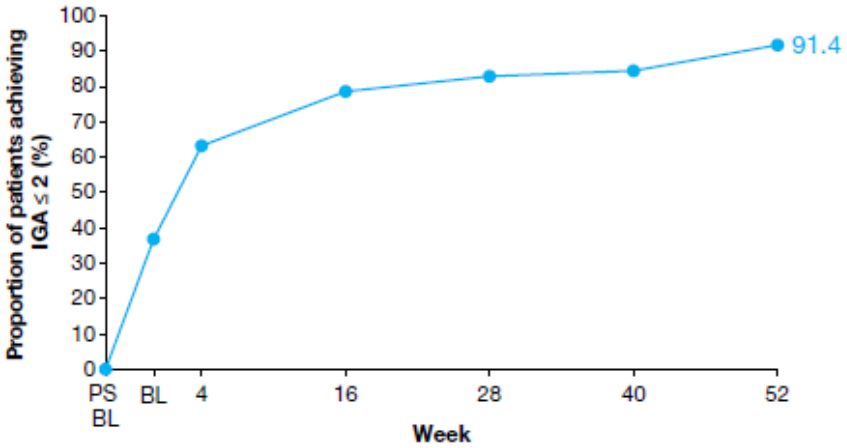

≥ 5 kg to < 15 kg (n = 39)
15 kg to < 30 kg (n = 103)
a
Proportion of patients achieving IGA 0/1 (%)
100
90
80
70
60
50
40
30
20
10
0
41.2%
34.1%
PS BL
BL
4
16
28
40
52
Week
No. of patients at visit
39 38 38 37 32 17
103 101 101 100 82 41
b
Proportion of patients achieving EASI-75 (%)
82.4%
78.0%
No. of patients at visit
39 38 38 37 32 17
103 101 101 100 80 41
c
Mean % change (± SD) in EASI from PSBL
0
−20
−40
−60
−80
−100
−86.5%
−87.6%
No. of patients at visit
39 38 38 37 32 17
103 101 101 100 80 41

Fig. S2 Other efficacy outcomes from PSBL through week 52 of the PED-OLE.

(a) Proportion of patients who achieved IGA ≤ 2 (PSBL to week 52 of the OLE), (b) Mean EASI (PSBL to week 52 of the OLE), (c) Mean change in EASI from PSBL to week 52 of the OLE

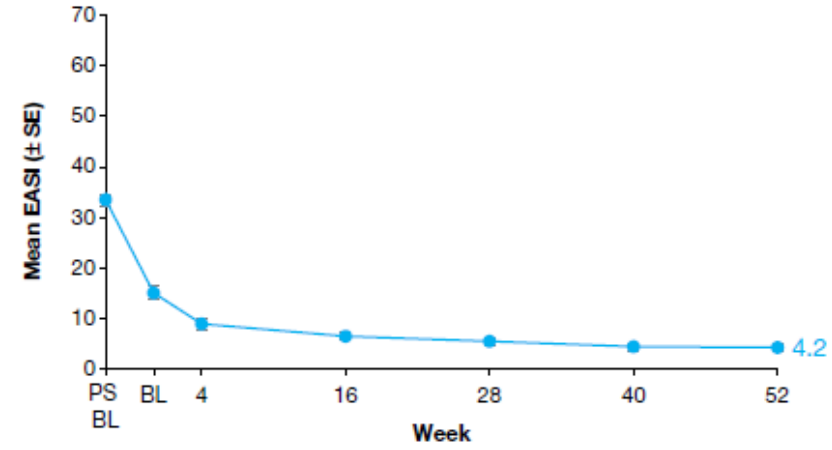
BL baseline of OLE, *EASI* Eczema Area and Severity Index, *IGA* Investigator's Global Assessment, *OLE* open-label extension, *PSBL* parent study baseline, *SD* standard deviation, *SE* standard error

a



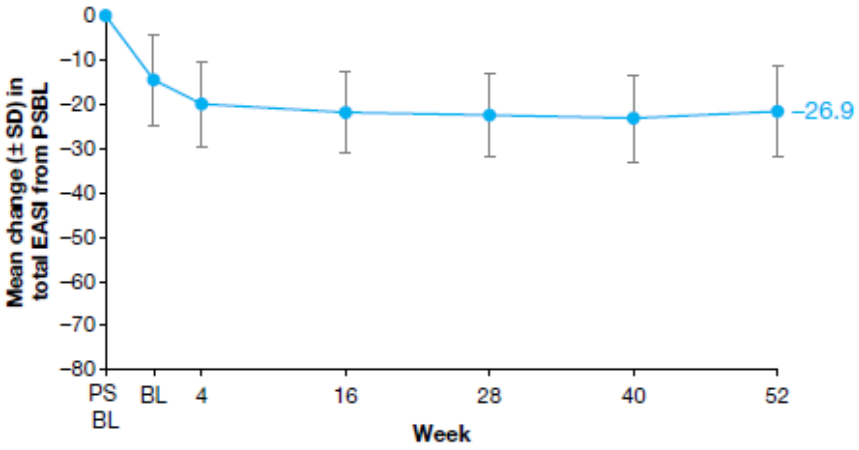
No. of patients at visit	142	139	139	137	114	58

b



No. of patients at visit	142	139	139	137	112	58

c



No. of patients at visit	142	139	139	137	112	58

Supplementary tables

Table S1 Patient demographics and clinical characteristics at baseline of PED-OLE by weight group and age group

	Baseline body weight group		**Age group**	
	≥ 5 kg to < 15 kg (*n* = 39)	**≥ 15 kg to < 30 kg (*n* = 103)**	**6 months to < 2 years (*n* = 7)**	**2 to < 6 years (*n* = 135)**
Age, years, mean (SD)	3.0 (1.1)	4.5 (0.8)	1.4 (0.2)	4.2 (1.0)
Sex, male, *n* (%)	22 (56.4)	67 (65.0)	6 (85.7)	83 (61.5)
Country, *n* (%)				
Germany	0	2 (1.9)	0	2 (1.5)
Poland	9 (23.1)	25 (24.3)	3 (42.9)	31 (23.0)
United Kingdom	2 (5.1)	6 (5.8)	1 (14.3)	7 (5.2)
United States	28 (71.8)	70 (68.0)	3 (42.9)	95 (70.4)
Race, *n* (%)				
White	29 (74.4)	64 (62.1)	7 (100.0)	86 (63.7)
Black or African American	4 (10.3)	22 (21.4)	0	26 (19.3)
Asian	2 (5.1)	8 (7.8)	0	10 (7.4)
Native Hawaiian or Other Pacific Islander	1 (2.6)	0	0	1 (0.7)
Other	3 (7.7)	3 (2.9)	0	6 (4.4)
Not reported	0	6 (5.8)	0	6 (4.4)
Ethnicity, *n* (%)				

	Baseline body weight group		**Age group**	
	≥ 5 kg to < 15 kg (*n* = 39)	**≥ 15 kg to < 30 kg (*n* = 103)**	**6 months to < 2 years (*n* = 7)**	**2 to < 6 years (*n* = 135)**
Not Hispanic or Latino	34 (87.2)	86 (83.5)	6 (85.7)	114 (84.4)
Hispanic or Latino	5 (12.8)	14 (13.6)	1 (14.3)	18 (13.3)
Not reported	0	3 (2.9)	0	3 (2.2)
Weight, kg, mean (SD)	13.1 (1.4)	19.2 (3.1)	10.9 (1.2)	17.8 (3.7)
BMI, kg/m^2, mean (SD)	15.8 (1.9)	16.4 (1.7)	17.9 (1.6)	16.2 (1.8)
Duration of AD, years, mean (SD)	2.7 (1.1)	4.0 (1.0)	1.1 (0.3)	3.8 (1.1)
IGA, *n* (%)				
0	3 (7.7)	1 (1.0)	1 (14.3)	3 (2.2)
1	3 (7.7)	14 (13.6)	1 (14.3)	16 (11.9)
2	6 (15.4)	25 (24.3)	2 (28.6)	29 (21.5)
3	19 (48.7)	41 (39.8)	1 (14.3)	59 (43.7)
4	8 (20.5)	22 (21.4)	2 (28.6)	28 (20.7)
EASI, mean (SD)	17.4 (15.0)	14.2 (12.5)	16.6 (17.4)	15.0 (13.1)
Percent BSA affected by AD, mean (SD)	32.2 (23.5)	26.1 (18.8)	33.9 (26.5)	27.4 (20.0)
SCORAD, mean (SD)	44.3 (24.6)	43.1 (21.4)	46.0 (35.5)	43.3 (21.5)
CDLQI, mean (SD)	10.2 (5.5) (*n* = 6)	9.9 (7.0) (*n* = 79)	N/A	9.9 (6.9) (*n* = 85)

	Baseline body weight group		**Age group**	
	≥ 5 kg to < 15 kg (*n* = 39)	**≥ 15 kg to < 30 kg (*n* = 103)**	**6 months to < 2 years (*n* = 7)**	**2 to < 6 years (*n* = 135)**
IDQOL, mean (SD)	10.3 (7.3) (*n* = 33)	8.8 (7.1) (*n* = 24)	10.9 (10.8) (*n* = 7)	9.5 (6.7) (*n* = 50)
Patients with ongoing or history of allergic/atopic conditions at baseline (excluding AD), *n* (%)	39 (100.0)	103 (100.0)		
Food allergy	27 (69.2)	69 (67.0)	3 (42.9)	98 (72.6)
Other allergies	19 (48.7)	55 (53.4)	1 (14.3)	77 (57.0)
Allergic rhinitis	17 (43.6)	44 (42.7)	1 (14.3)	62 (45.9)
Hives	12 (30.8)	23 (22.3)	2 (28.6)	37 (27.4)
Asthma	7 (17.9)	27 (26.2)	0	36 (26.7)
Allergic conjunctivitis	2 (5.1)	6 (5.8)	0	8 (5.9)
Chronic rhinosinusitis	0	3 (2.9)	0	3 (2.2)
Eosinophilic esophagitis	0	2 (1.9)	0	3 (2.2)
Patients receiving prior systemic medications for AD, *n* (%)[a]	17 (43.6)	34 (33.0)	2 (28.6)	49 (36.3)
Patients receiving prior systemic corticosteroids	9 (23.1)	27 (26.2)	2 (28.6)	34 (25.2)

	Baseline body weight group		**Age group**	
	≥ 5 kg to < 15 kg (*n* = 39)	**≥ 15 kg to < 30 kg (*n* = 103)**	**6 months to < 2 years (*n* = 7)**	**2 to < 6 years (*n* = 135)**
Patients receiving prior systemic non-steroidal immunosuppressants	17 (43.6)	28 (27.2)	2 (28.6)	24 (17.8)
Cyclosporine	6 (15.4)	11 (10.7)	1 (14.3)	16 (11.9)
Methotrexate	6 (15.4)	6 (5.8)	0	12 (8.9)
Mycophenolate	0	4 (3.9)	0	4 (3.0)
Azathioprine	0	2 (1.9)	0	2 (1.5)

AD atopic dermatitis, *BMI* body mass index, *BSA* body surface area, *CDLQI* Children's Dermatology Life Quality Index, *EASI* Eczema Area and Severity Index, *IDQOL* Infants' Dermatitis Quality of Life Index, *IGA* Investigator's Global Assessment, *SCORAD* SCORing Atopic Dermatitis, *SD* standard deviation

[a]Patients may have received more than 1 type of prior systemic medication.

Table S2 Serious treatment-emergent adverse events over 52 weeks in the PED-OLE

Treatment received in previous study	Treatment received in OLE	Age	Sex	Baseline weight (kg)	Reported term for the AE	Dictionary-derived term	Severity/ Intensity	Serious event	Action taken with study treatment	Causality	Outcome of AE	Duration of AE (days)	AE ongoing? (Y/N)	Last dose before or on AE start date
Dupilumab 200 mg q4w	Dupilumab 200 or 300 mg q4w	2.6	M	13.2	PINWORM	Enterobiasis	MODERATE	Y	DOSE NOT CHANGED	RELATED	RECOVERED/ RESOLVED	15	N	200 mg q4w
Dupilumab 300 mg q4w	Dupilumab 200 or 300 mg q4w	5.3	F	21.0	REHABILITATION IN A MOTHER-CHILD HEALTH RESORT DUE TO ATOPIC DERMATITIS	Dermatitis atopic	MILD	Y	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	16	N	300 mg q4w
Dupilumab 300 mg q4w	Dupilumab 200 or 300 mg q4w	4.0	F	18.0	HYPERTROPHY OF THE PHARYNGEAL TONSIL	Adenoidal hypertrophy	MODERATE	Y	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	5	N	300 mg q4w
Dupilumab 300 mg q4w	Dupilumab 200 or 300 mg q4w	4.0	F	18.0	HYPERTROPHY OF THE PALATINE TONSILS	Tonsillar hypertrophy	MODERATE	Y	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	5	N	300 mg q4w
Dupilumab 300 mg q4w	Dupilumab 200 or 300 mg q4w	4.4	M	19.7	VIRAL GASTRO-ENTERITIS	Gastroenteritis viral	MODERATE	Y	NOT APPLICABLE	NOT RELATED	RECOVERED/ RESOLVED	2	N	300 mg q4w
Dupilumab 300 mg q4w	Dupilumab 200 or 300 mg q4w	4.7	M	15.9	PERIORBITAL CELLULITIS (PAIN, SWELLING, REDNESS)	Periorbital cellulitis	MODERATE	Y	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	9	N	300 mg q4w

Placebo	Dupilumab 200 or 300 mg q4w	3.1	M	13.2	NON-SUPPURATIVE OTITIS MEDIA	Otitis media	MILD	Y	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	3	N	200 mg q4w
Placebo	Dupilumab 200 or 300 mg q4w	3.5	M	16.5	ACUTE PURULENT OTITIS MEDIA (BOTH EARS)	Otitis media acute	SEVERE	Y	DRUG INTERRUPTED	NOT RELATED	RECOVERED/ RESOLVED	10	N	300 mg q4w
Placebo	Dupilumab 200 or 300 mg q4w	4.7	F	17.7	DIABETIC KETOACIDOSIS	Diabetic ketoacidosis	SEVERE	Y	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED WITH SEQUELAE	4	N	300 mg q4w

AE adverse event, *OLE* open-label extension, *q4w* every 4 weeks

Table S3 Treatment-emergent adverse events leading to treatment discontinuation over 52 weeks in the PED-OLE

Treatment received in previous study	Treatment received in OLE	Age	Sex	Baseline weight (kg)	Reported term for the AE	Dictionary-derived term	Severity/ Intensity	Serious event	Action taken with study treatment	Causality	Outcome of AE	Duration of AE (days)	AE ongoing? (Y/N)	Last dose before or on AE start date
Dupilumab 300 mg q4w	Dupilumab 200 or 300 mg q4w	4.8	M	25.5	URTICARIA	Urticaria	SEVERE	N	DRUG WITHDRAWN	RELATED	RECOVERED / RESOLVED	1	N	300 mg q4w

AE adverse event, *OLE* open-label extension, *q4w* every 4 weeks

Table S4 Treatment-emergent adverse events of special interest over 52 weeks in the PED-OLE

Treatment received in previous study	Treatment received in OLE	Age	Sex	Baseline weight (kg)	Reported term for the AE	Dictionary-derived term	Severity/ Intensity	Serious event	Action taken with study treatment	Causality	Outcome of AE	Duration of AE (days)	AE ongoing? (Y/N)	Last dose before or on AE start date
Dupilumab 200 mg q4w	Dupilumab 200 mg q4w	2.6	M	13.2	ANAPHYLAXIS	Anaphylactic reaction	MODERATE	N	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	1	N	200 mg q4w
Dupilumab 200 mg q4w	Dupilumab 200 mg q4w	2.6	M	13.2	PINWORM	Enterobiasis	MODERATE	Y	DOSE NOT CHANGED	RELATED	RECOVERED/ RESOLVED	15	N	200 mg q4w
Dupilumab 300 mg q4w	Dupilumab 300 mg q4w	4.8	F	17.1	BILATERAL ULCERATING BLEPHARITIS	Blepharitis	SEVERE	N	DOSE NOT CHANGED	RELATED	RECOVERED/ RESOLVED	43	N	300 mg q4w
Placebo	Dupilumab 300 mg q4w	4.4	M	15.5	PHLYCTENULAR CONJUNCTIVITIS OF BOTH EYES	Keratitis	MODERATE	N	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	23	N	300 mg q4w
Placebo	Dupilumab 200 mg q4w	1.4	M	11.2	ANAPHYLACTIC REACTION	Anaphylactic reaction	MODERATE	N	DOSE NOT CHANGED	NOT RELATED	RECOVERED/ RESOLVED	1	N	200 mg q4w

AE adverse event, *OLE* open-label extension, *q4w* every 4 weeks

Table S5 Safety assessment over 52 weeks in the PED-OLE: conjunctivitis

	All patients (*N* =142)		
	nP (%)[a]	**nP/100PY[a]**	**nE (nE/100PY)**
Treatment-emergent conjunctivitis[b]	18 (12.7)	14.6	21 (15.9)
Conjunctivitis allergic (PT)	8 (5.6)	6.3	10 (7.6)
Conjunctivitis (PT)	5 (3.5)	3.9	5 (3.8)
Conjunctivitis bacterial (PT)	5 (3.5)	3.8	5 (3.8)
Conjunctivitis viral (PT)	1 (0.7)	0.8	1 (0.8)
Atopic keratoconjunctivitis (PT)	0	0	0
Conjunctivitis SAE	0	0	0
Conjunctivitis by severity			
Mild	9 (6.3)	–	9 (6.8)
Moderate	9 (6.3)	–	12 (9.1)
Severe	0	–	0
Conjunctivitis leading to treatment discontinuation	0	–	0
Conjunctivitis by outcome			
Recovered/Resolved	12 (8.5)	–	14 (10.6)
Recovering/Resolving	0	–	0
Ongoing	6 (4.2)	–	7 (5.3)
Prior history of conjunctivitis[b]			
In parent study, n/N1 (%)	15/18 (83.3)	–	–
Prior to parent study, n/N1 (%)	5/18 (27.8)	–	–

MedDRA Medical Dictionary for Regulatory Activities, *N1* patients with non-missing scores at each week, *nE* number of events, *nE/100PY* nE per 100 patient-years, *nP* number of patients, *nP/100PY* nP per 100 patient-years, *PT* MedDRA Preferred Term, *SAE* serious adverse event

[a]Patients may have had more than one event

[b]Conjunctivitis (narrow) includes PTs conjunctivitis, bacterial conjunctivitis, viral conjunctivitis, allergic conjunctivitis, and atopic keratoconjunctivitis

Table S6 Safety assessment over 52 weeks in the PED-OLE: skin infections

	All patients (*N* = 142)	
	***n* (%)**	**nP/100PY**
Infections and infestations (SOC)	35 (24.6)	30.4
Herpes viral infections (HLT)	14 (9.9)	11.0
Herpes simplex (PT)	4 (2.8)	3.1
Oral herpes (PT)	4 (2.8)	3.1
Varicella (PT)	4 (2.8)	3.1
Herpes ophthalmic (PT)	1 (0.7)	0.8
Herpes virus infection (PT)	1 (0.7)	0.8
Skin structures and soft tissue infections (HLT)	10 (7.0)	7.9
Impetigo (PT)	5 (3.5)	3.9
Skin infection (PT)	4 (2.8)	3.1
Dermatitis infected (PT)	1 (0.7)	0.8
Enteroviral infections NEC	4 (2.8)	3.1
Hand-foot-and-mouth disease	4 (2.8)	3.1
Molluscum contagiosum viral infections (HLT)	3 (2.1)	2.3
Molluscum contagiosum (PT)	3 (2.1)	2.3
Staphylococcal infections (HLT)	3 (2.1)	2.3
Furuncle (PT)	1 (0.7)	0.8
Staphylococcal infection (PT)	1 (0.7)	0.8
Staphylococcal skin infection (PT)	1 (0.7)	0.8
Echo viral infections	2 (1.4)	1.5
Boston exanthema (PT)	2 (1.4)	1.5
Tinea infections	2 (1.4)	1.5
Tinea capitis (PT)	1 (0.7)	0.8
Tinea pedis (PT)	1 (0.7)	0.8

	All patients (*N* = 142)	
	***n* (%)**	**nP/100PY**
Viral infections NEC	2 (1.4)	1.5
Viral skin infection (PT)	2 (1.4)	1.5
Bacterial infections NEC	1 (0.7)	0.8
Eczema impetiginous (PT)	1 (0.7)	0.8
Fungal infections NEC	1 (0.7)	0.8
Fungal skin infection (PT)	1 (0.7)	0.8

HLT MedDRA High Level Term, *MedDRA* Medical Dictionary for Regulatory Activities, *NEC* not otherwise specified, *nP/100PY* number of patients per 100 patient-years, *PT* MedDRA Preferred Term, *SOC* MedDRA system organ class

Table S7 Safety assessment by age group in the PED-OLE

	6 months to < 2 years (*n* = 7)		**2 to < 6 years (*n* = 135)**	
	nE	**nE/100PY**	**nE**	**nE/100PY**
Total number of TEAEs	28	422.3	491	392.5
Total number of serious TEAEs	0	0	9	7.2
Total number of severe TEAEs	0	0	6	4.8
Total number of TEAEs related to treatment	0	0	28	22.4
Total number of TEAEs leading to permanent treatment discontinuation[a]	0	0	1	0.8
Patients with:	***n* (%)**	**nP/100PY**	***n* (%)**	**nP/100PY**
Any TEAE	7 (100.0)	427.6	104 (77.0)	198.0
Any serious TEAE	0	0	8 (5.9)	6.5
Any severe TEAE	0	0	6 (4.4)	4.9
Any TEAEs related to treatment	0	0	18 (13.3)	15.6
Any TEAEs leading to permanent discontinuation	0	0	1 (0.7)	0.8
Conjunctivitis cluster[b]	1 (14.3)	15.7	17 (12.6)	14.6
Injection-site reactions (HLT)	0	0	3 (2.2)	2.4

Skin infections (SOC) (excluding herpes viral infections)	1 (14.3)	17.9	23 (17.0)	20.3
Herpes viral infections (HLT)	0	0	14 (10.4)	11.6
Hand-foot-and-mouth disease (PT)	0	0	4 (3.0)	3.2
Skin papilloma (PT)	0	0	4 (3.0)	3.2
Most common TEAEs reported in ≥ 3% of all patients (PT): [c]				
Nasopharyngitis	1 (14.3)	17.3	27 (20.0)	24.3
Cough	1 (14.3)	16.7	21 (15.6)	18.4
Pyrexia	1 (14.3)	16.6	19 (14.1)	16.4
COVID-19	1 (14.3)	15.5	19 (14.1)	15.9
Dermatitis atopic	0	0	16 (11.9)	13.6
Upper respiratory tract infection	1 (14.3)	16.7	14 (10.4)	12.1
Rhinorrhea	0	0	12 (8.9)	10.1
Conjunctivitis allergic	1 (14.3)	15.7	7 (5.2)	5.8
Diarrhea	0	0	8 (5.9)	6.6
Urticaria	0	0	7 (5.2)	5.8
Vomiting	0	0	7 (5.2)	5.8
Ear infection	0	0	6 (4.4)	4.9
Asthma	0	0	5 (3.7)	4.1
Conjunctivitis	0	0	5 (3.7)	4.1
Impetigo	1 (14.3)	17.9	4 (3.0)	3.2
Conjunctivitis bacterial	0	0	5 (3.7)	4.0

Otitis media	0	0	5 (3.7)	4.0

HLT MedDRA High Level Term, *MedDRA* Medical Dictionary for Regulatory Activities, *nE* number of events, *nE/100PY*, nE per 100 patient-years, *nP/100PY* number of patients per 100 patient-years, *PT* MedDRA Preferred Term, *SOC* MedDRA System Organ Class, *TEAE* treatment-emergent adverse event

[a]Patient discontinued due to TEAE of severe urticaria

[b]Conjunctivitis cluster includes conjunctivitis, bacterial conjunctivitis, viral conjunctivitis, allergic conjunctivitis, and atopic keratoconjunctivitis

[c]TEAEs shown in this table are those occurring in ≥ 3% of the full safety analysis set (*N* = 142), presented by age group

Table S8 Efficacy assessment at weeks 4, 16, and 52 of the PED-OLE by age group

	6 months to < 2 years (*n* = 7)			**2 to < 6 years (*n* = 135)**		
	Week 4 (*n* = 7)	**Week 16 (*n* = 7)**	**Week 52 (*n* = 3)**	**Week 4 (*n* = 132)**	**Week 16 (*n* = 132)**	**Week 52 (*n* = 55)**
Proportion of patients achieving IGA 0 or 1, *n* (%)	3 (42.9)	5 (71.4)	1 (33.3)	32 (24.2)	45 (34.1)	20 (36.4)
Proportion of patients achieving EASI-50, *n* (%)	6 (85.7)	6 (85.7)	3 (100)	113 (85.6)	120 (90.9)	53 (96.4)
Proportion of patients achieving EASI-75, *n* (%)	5 (71.4)	6 (85.7)	3 (100)	82 (62.1)	98 (74.2)	43 (78.2)
Proportion of patients achieving EASI-90, *n* (%)	5 (71.4)	5 (71.4)	3 (100)	48 (36.4)	59 (44.7)	31 (56.4)
Percentage change from baseline of parent study in EASI, mean (SD)	−75.5 (41.1)	−89.3 (19.3)	−94.9 (2.7)	−74.9 (23.3)	−81.8 (18.9)	−86.2 (16.7)
Change from baseline of parent study in EASI, mean (SD)	−33.3 (24.9)	−37.7 (21.9)	−34.6 (20.9)	−24.4 (10.7)	−26.8 (10.3)	−26.4 (12.2)
Change from baseline of parent study in percent BSA	−46.1 (38.2)	−59.6 (24.3)	−47.7 (15.9)	−39.6 (21.5) (*n* = 131)	−44.5 (19.4)	−45.5 (22.9)

	6 months to < 2 years (*n* = 7)			**2 to < 6 years (*n* = 135)**		
	Week 4 (*n* = 7)	**Week 16 (*n* = 7)**	**Week 52 (*n* = 3)**	**Week 4 (*n* = 132)**	**Week 16 (*n* = 132)**	**Week 52 (*n* = 55)**
affected by AD, mean (SD)						
Percentage change from baseline of parent study SCORAD, mean (SD)	−61.8 (43.2)	−74.0 (29.5)	−77.3 (9.8)	−57.2 (24.1) (*n* = 130)	−65.4 (20.5) (*n* = 131)	−69.9 (21.8)
Change from baseline of parent study in CDLQI, mean (SD)	n/a	–	n/a	−11.1 (6.9) (*n* = 66)	–	−13.7 (6.4) (*n* = 30)
Proportion of patients with ≥ 6-point improvement in CDLQI, n/N1 (%)[a]	n/a	–	n/a	54/66 (81.8)	–	27/30 (90.0)
Change from baseline of parent study in IDQOL, mean (SD)	−11.6 (6.7)	–	−17.3 (3.2) (*n* = 3)	−10.2 (6.4) (*n* = 48)	–	−14.0 (4.6) (*n* = 7)
Proportion of patients with ≥ 6-point improvement in IDQOL, n/N1 (%)[a]	6/7 (85.7)	–	3/3 (100)	40/47 (85.1)	–	7/7 (100)

AD atopic dermatitis, *BSA* body surface area, *CDLQI* Children's Dermatology Life Quality Index, *EASI* Eczema Area and Severity Index, *EASI-50/75/90* patients achieving a 50%/75%/90% reduction, respectively, in EASI compared with PSBL, *IDQOL* Infants' Dermatitis Quality of Life

Index, *IGA* Investigator's Global Assessment, *N1* patients with non-missing scores at each week, *n/a* not applicable, *OLE* open-label extension, *PSBL* parent study baseline, *SCORAD* SCORing Atopic Dermatitis, *SD* standard deviation

[a]Among patients with CDLQI ≥ 6 at PSBL or IDQOL ≥ 6 at PSBL

Appendix S1 Eligibility criteria

Inclusion Criteria for the Phase 3 Open-Label Extension

- Male or female, aged ≥ 6 months to < 18 years at the time of screening (NOTE: patients who turned age 18 years during a prior study were not eligible to enroll in this study but may have been eligible to enroll into the adult open-label extension [OLE] study [R668-AD-1225], if it was still ongoing)
- Participated in a prior dupilumab study in pediatric patients with atopic dermatitis (AD) and adequately completed the visits and assessments required for both the treatment and follow-up periods, as defined in the prior study protocol. Specifically, patients needed to meet the criterion below:
  - Patients from study R668-AD-1539 need to have completed at least 50% of visits (in-clinic and/or phone visits) during the treatment and follow-up periods as defined in the parent protocols, including completing the study assessments and procedures planned for each of those visits
  - Completion of the follow-up period is not required for parent studies when the protocol specifically allows for an earlier transition into the OLE at the end of the treatment period, and these patients need to have completed at least 50% of visits (in-clinic and/or phone visits) during the treatment period as defined in the parent protocols, including completing the study assessments and procedures that are applicable to them, planned for each of those visits
  - These patients need to meet the criteria for early transition into the OLE, which will be specified in the parent protocol. Patients who discontinued a parent study prematurely (i.e., patients who did not complete the protocol-defined end-of-study visit) cannot enroll into this OLE study before the date when the patient would have been allowed to transition into OLE as per the requirements of the parent protocol
- Willing and able to comply with all clinic visits and study-related procedures
- Patient (either alone or with the help of their parents/legal guardians, as appropriate) must have been able to understand and complete study-related questionnaires

- Parent(s) or legal guardian(s) must have provided the signed ICF
- Patients aged ≥ 7 years (or above an age determined by the IRB/EC and in accordance with local regulations and requirements) must have also provided informed assent forms (IAFs) to enroll in the study, and sign and date either a separate IAF or the ICF signed by the parent(s)/legal guardian(s) (as appropriate, based on local regulations and requirements)

Exclusion Criteria for the Phase 3 Open-Label Extension

- Patients who developed a serious adverse event deemed related to study drug during their participation in a prior dupilumab study in pediatric patients with AD that, in the opinion of the investigator or of the medical monitor, could have indicated that continued treatment with study drug may present an unreasonable risk for the patient
- Patients who developed an adverse event that was deemed related to study drug and led to study treatment discontinuation during their participation in a prior dupilumab study in pediatric patients with AD that, in the opinion of the investigator or of the medical monitor, could have indicated that continued treatment with study drug may present an unreasonable risk for the patient
- Patients who were prematurely withdrawn from a prior dupilumab study in pediatric patients with AD by the investigator because of non-compliance and/or inability to complete required study assessments
- Patients who were treated with an investigational drug other than dupilumab within 8 weeks or within 5 half-lives (if known), whichever was longer, before the baseline visit.
- Patients who have used the following treatments within 4 weeks before the baseline visit:
  - Systemic corticosteroids
  - Immunosuppressive/immunomodulating drugs (i.e., cyclosporine, mycophenolate mofetil, IFN-γ, Janus kinase inhibitors, azathioprine, or methotrexate)
  - Phototherapy

- Treatment with biologics other than dupilumab as follows:
  - Any cell-depleting agents including (but not limited to) rituximab: within 6 months before the baseline visit, or until lymphocyte and CD 19+ lymphocyte count returned to normal, whichever was longer
  - Other biologics: within 5 half-lives (if known) or 16 weeks prior to the baseline visit, whichever was longer
- Planned or anticipated use of any prohibited medications and procedures during study treatment
- Treatment with a live (attenuated) vaccine within 4 weeks before the baseline visit (NOTE: For patients who had vaccination with live, attenuated vaccines planned during the course of the study [based on national vaccination schedule/local guidelines], it was determined, after consultation with a pediatrician, whether the administration of the vaccine could be postponed until after the end of study, or moved to before the start of the study, without compromising the health of the patient):
  - Patients for whom administration of live (attenuated) vaccine could be safely postponed would be eligible to enroll into the study
  - Patients who had their vaccination moved to before the start of the study could enroll in the study only after a gap of 4 weeks following administration of the vaccine
- Patients with body weight at baseline of < 5 kg
- Known or suspected immunodeficiency, including history of invasive opportunistic infections (i.e., tuberculosis, histoplasmosis, listeriosis, coccidioidomycosis, pneumocystosis, aspergillosis) despite infection resolution, or otherwise recurrent infections of abnormal frequency or prolonged duration that suggested an immune compromised status, as judged by the investigator
- Patients with an established diagnosis of a primary immunodeficiency disorder (i.e., Severe Combined Immunodeficiency, DiGeorge Syndrome, X-linked Agammaglobulinemia, and Common Variable Immunodeficiency)

- Patients who presented with eczema as part of a genodermatotic syndrome like Netherton's syndrome, Hyper IgE syndrome, Wiskott–Aldrich syndrome, etc.
- Known history of human immunodeficiency virus (HIV) infection or HIV seropositivity at the screening visit
  - Note: HIV serology was performed in patients who did not have this test performed during participation in the previous study
- With an established diagnosis of hepatitis B viral infection at the time of screening or was positive for hepatitis B surface antigen (HBsAg) or hepatitis B core antibody (HBcAb) at the time of screening
  - Note: Hepatitis B virus (HBV) serology was only performed in patients who did not have this test performed during participation in the previous study
- Patients who had gained immunity for HBV infection after vaccination (patients who were HBsAg negative, hepatitis B surface antibody positive, and HBcAb negative) were eligible for the study
  - These patients were allowed to enroll into the study but were followed using routine clinical and liver function tests
- Patients with an established diagnosis of hepatitis C viral infection at the time of screening or who were positive for hepatitis C antibody at the screening visit
  - Note: Hepatitis C virus serology was only performed in patients who did not have this test performed during participation in the parent study
- Patients who were on current treatment for hepatic disease, including (but not limited to) acute or chronic hepatitis, cirrhosis or hepatic failure, or had evidence of liver disease as indicated by persistent (confirmed by repeated tests ≥ 2 weeks apart) elevated transaminases (alanine aminotransferase [ALT] and/or aspartate aminotransferase [AST]) more than 3 times the upper limit of normal (ULN) during the screening period
- Presence of any 1 or more of the following abnormalities in laboratory test results at screening results:
  - Platelets ≤ $100 \times 10^3/\mu L$

  - Neutrophils < 1.5 × 10^3/µL for patients aged > 1 year; ≤ 1.0 × 10^3/µL for ≥ 6 months to < 1 year
  - Creatine phosphokinase (CPK) ≥ 5 × ULN
  - Serum creatinine > 1.5 × ULN
  - NOTE: If an abnormal value was detected at screening, a repeat test was performed to confirm the abnormality; if the repeat test confirmed the abnormality, the patient was categorized as a screen failure
- Presence of skin comorbidities (i.e., scabies, seborrheic dermatitis, psoriasis, and cutaneous T-cell lymphoma) that could have interfered with study assessments
- History of malignancy within 5 years of the baseline visit, except completely treated in situ carcinoma of the cervix and completely treated and resolved non-metastatic squamous or basal cell carcinoma of the skin
- History of non-malignant lymphoproliferative disorders
- History of clinical endoparasitosis (i.e., helminth infection) within 12 months before the baseline visit, or high risk of helminth infection, such as residence within or recent travel (within 12 months before the baseline visit) to areas endemic for endoparasitoses, where the circumstances were consistent with parasite exposure (i.e., extended stay; rural or slum areas; lack of running water; consumption of uncooked, undercooked, or otherwise potentially contaminated food; close contact with carriers and vectors; etc.), unless subsequent medical assessments (i.e., stool exam, blood tests, etc.) had ruled out the possibility of parasite infection/infestation
- History of alcohol or drug abuse within 2 years before the screening visit
- Severe concomitant illness(es) that, in the investigator's judgment, would have adversely affected the patient's participation in the study
  - Examples included (but were not limited to) patients with short life expectancy, uncontrolled diabetes (hemoglobin A1c ≥ 9%), cardiovascular conditions (i.e., Class III or IV cardiac failure according to the New York Heart Association classification), severe renal conditions (i.e., patients on dialysis), hepatobiliary conditions (i.e., Child–Pugh class B or C), neurological conditions (i.e.,

demyelinating diseases), active major autoimmune diseases (i.e., lupus, inflammatory bowel disease, rheumatoid arthritis, etc.), and other severe endocrinological, gastrointestinal, metabolic, pulmonary, or lymphatic diseases
  - The specific justification for patients excluded under this criterion was noted in study documents (chart notes, case report forms [CRFs], etc.)
- Any other medical or psychological condition including relevant laboratory abnormalities at screening that, in the opinion of the investigator, suggested a new and/or insufficiently understood disease, may have presented an unreasonable risk to the study patient as a result of his/her participation in this clinical trial, may make patient's participation unreliable, or could have interfered with study assessments
  - The specific justification for patients excluded under this criterion was noted in study documents (chart notes, CRFs, etc.)
- Planned major surgical procedure during the patient's participation in this study
- Patient or his/her immediate family member was a member of the investigational team
- Female patients who were pregnant, breastfeeding, or planning to become pregnant or breastfeed during the study
- Women of childbearing potential* who were unwilling to practice highly effective contraception prior to the initial dose/start of the treatment, during the study, and for at least 120 days after the last dose
  - This includes female patients who experience menarche during the study duration and who are unwilling to follow the precautions for women of childbearing potential
  - Highly effective contraceptive measures included stable use of combined (estrogen- and progestogen-containing) hormonal contraception (oral, intravaginal, transdermal) or progestogen-only hormonal contraception (oral, intravaginal, implantable) or progestogen-only hormonal contraception (oral injectable, implantable) associated with inhibition of ovulation initiated 2 or more menstrual cycles prior to screening; intrauterine device; intrauterine hormone-releasing system; and/or sexual abstinence**

        - *Defined as any female who is fertile following her first menstrual period (menarche), unless permanently sterile
        - **Sexual abstinence was considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments; reliability of sexual abstinence was evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the patient
    - Periodic abstinence (i.e., calendar, symptothermal, post-ovulation methods), withdrawal (coitus interruptus), spermicide-only, and lactational amenorrhea method (LAM) are not acceptable methods of contraception; female condom and male condom should not be used together
- Patients who were committed to an institution by virtue of an order issued either by the judicial or the administrative authorities