SUPPLEMENTARY INFORMATION

Title

The regulatory T cell-selective interleukin-2 receptor agonist rezpegaldesleukin in the treatment of inflammatory skin diseases: two randomized, double-blind, placebo-controlled phase 1b trials

Authors

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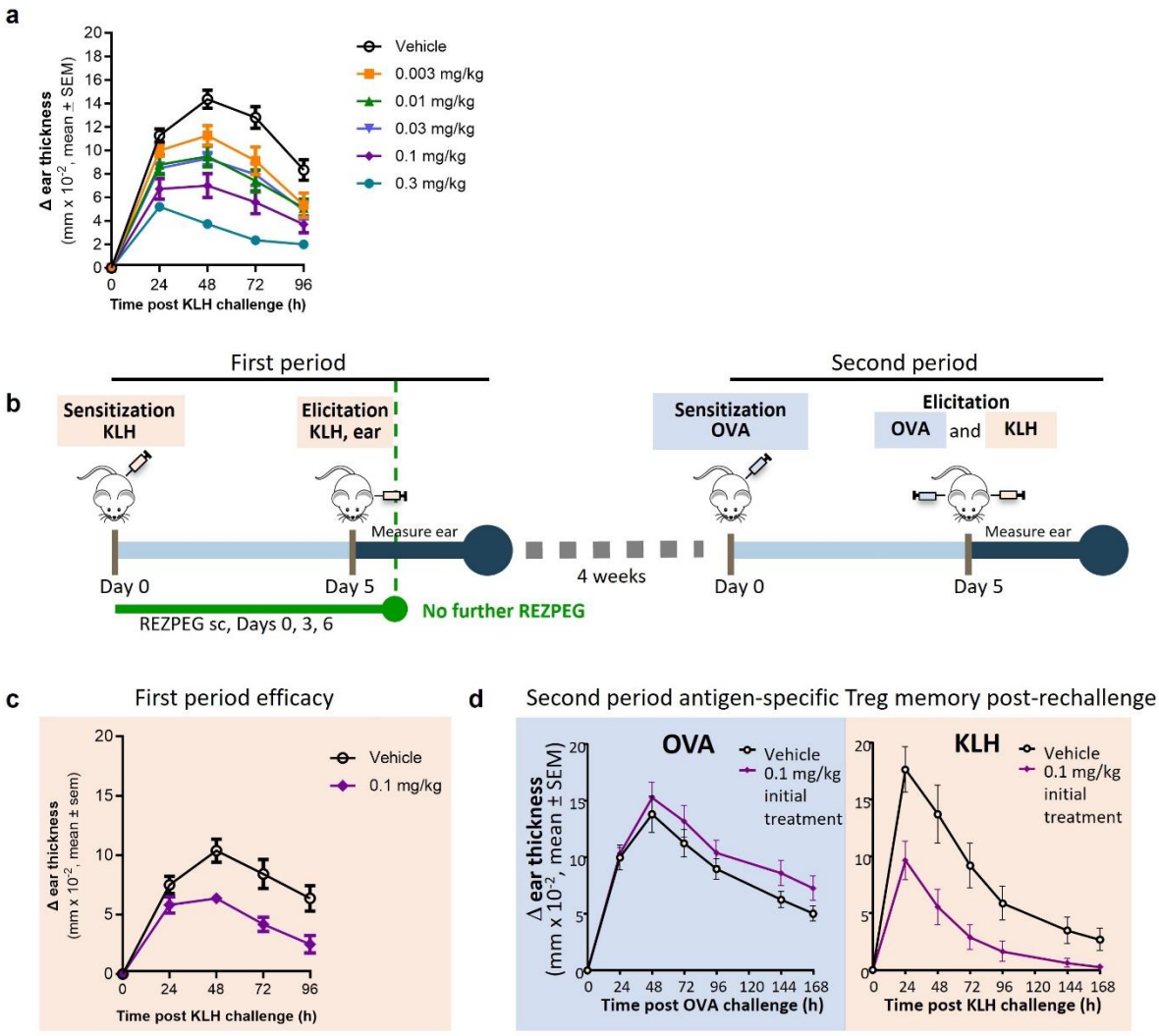
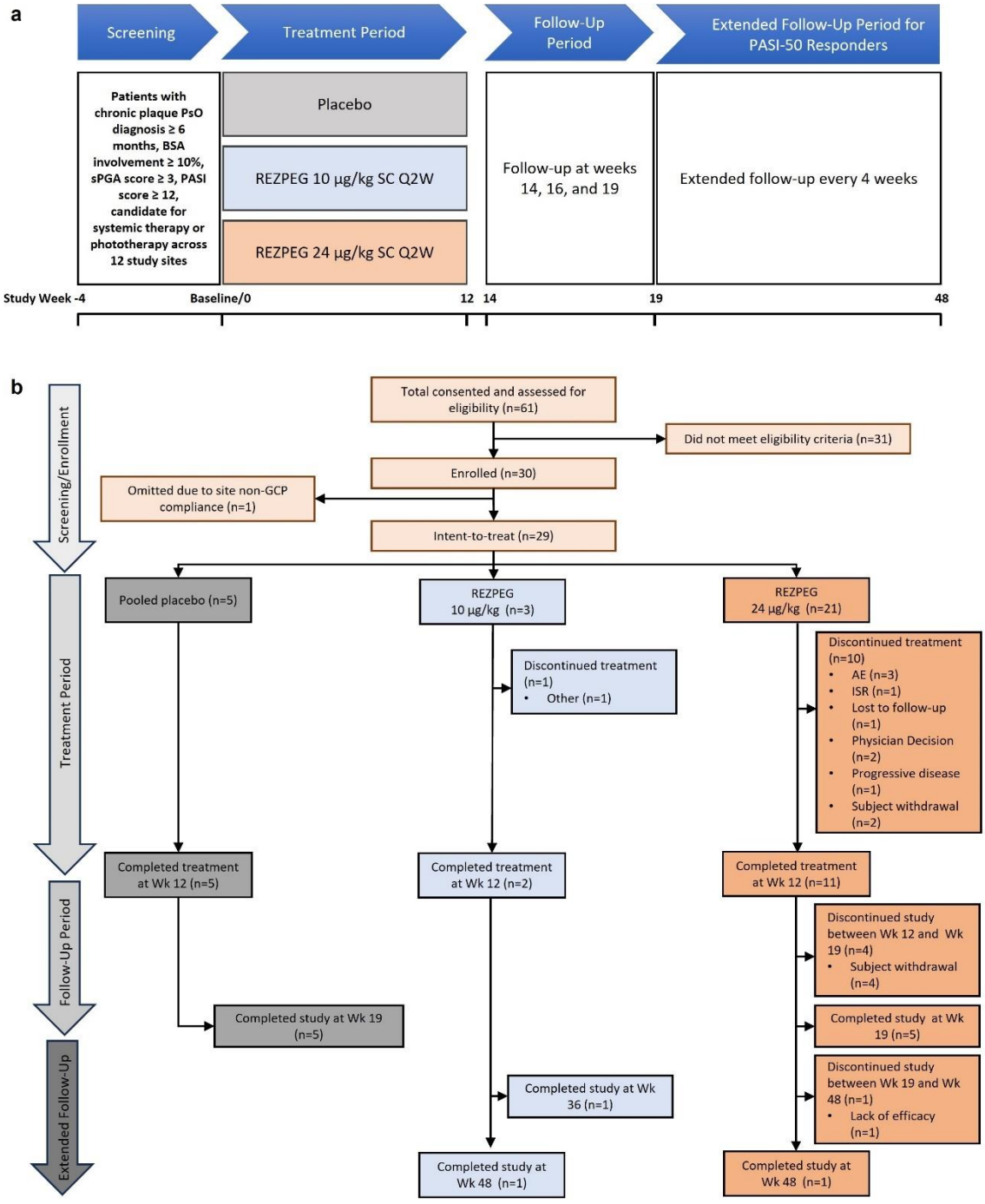


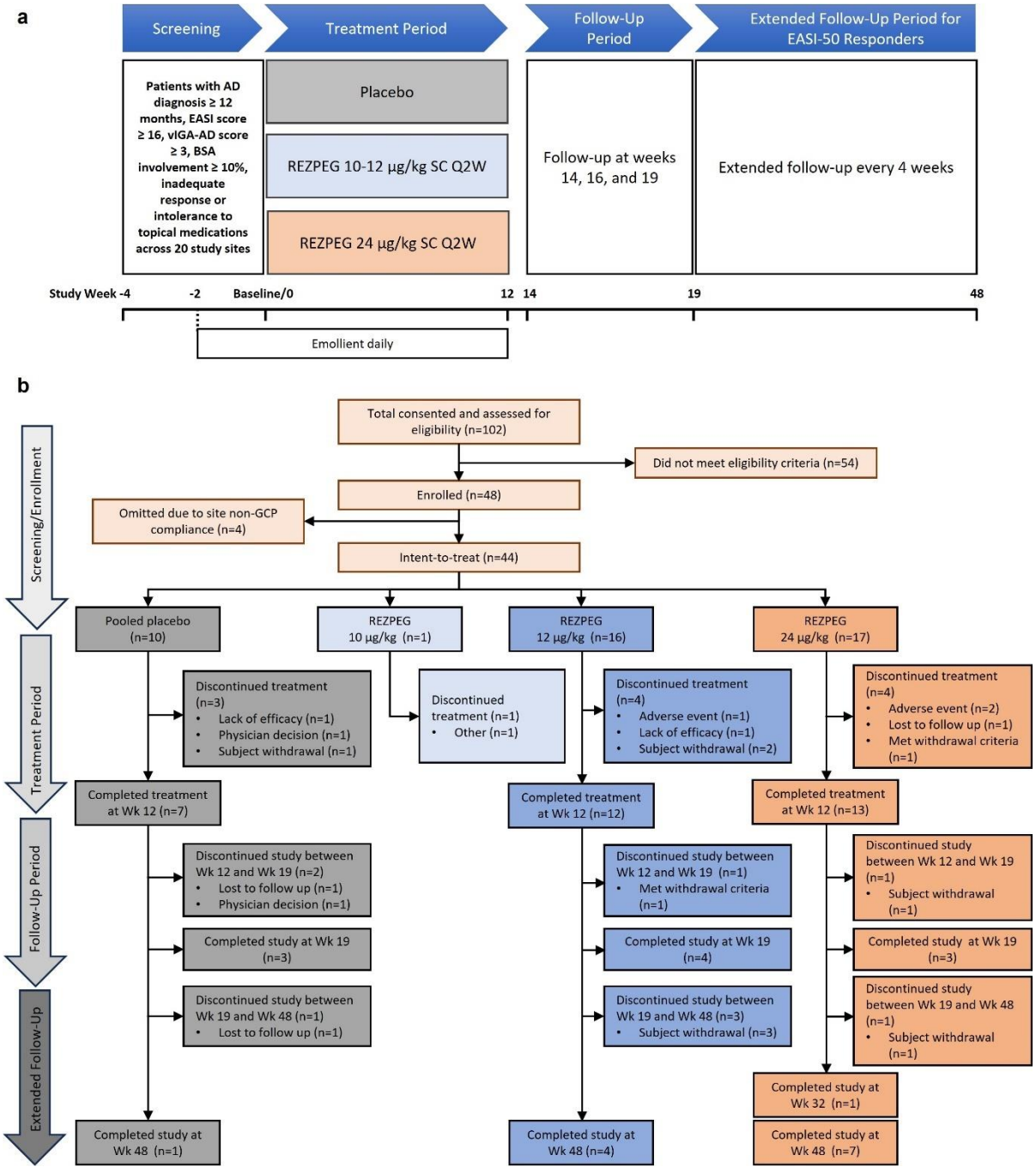
Supplementary Figure 1 | REZPEG reduces inflammation in DTH. Female BALB/c mice aged 6-8 weeks were used in the DTH model. **a**, REZPEG-induced dose-dependent reductions in ear thickness (n=10 per group). **b**, Study design for the antigen-specific mouse model of DTH. **c**, REZPEG-dependent reduction in ear thickness after KLH sensitization and challenge in the first period (n=8 per group). **d**, Reduction in antigen-specific ear thickness after OVA sensitization and challenge or KLH re-challenge in the second period (n=8 per group). Data shown as mean ± SEM. DTH, delayed-type hypersensitivity; KLH, keyhole limpet haemocyanin; OVA, ovalbumin; area and severity index; SEM, standard error of the mean; Tregs, regulatory T cells. Source data are provided as a Source Data file.

Supplementary Figure 2 | PsO study design and patient completion summary



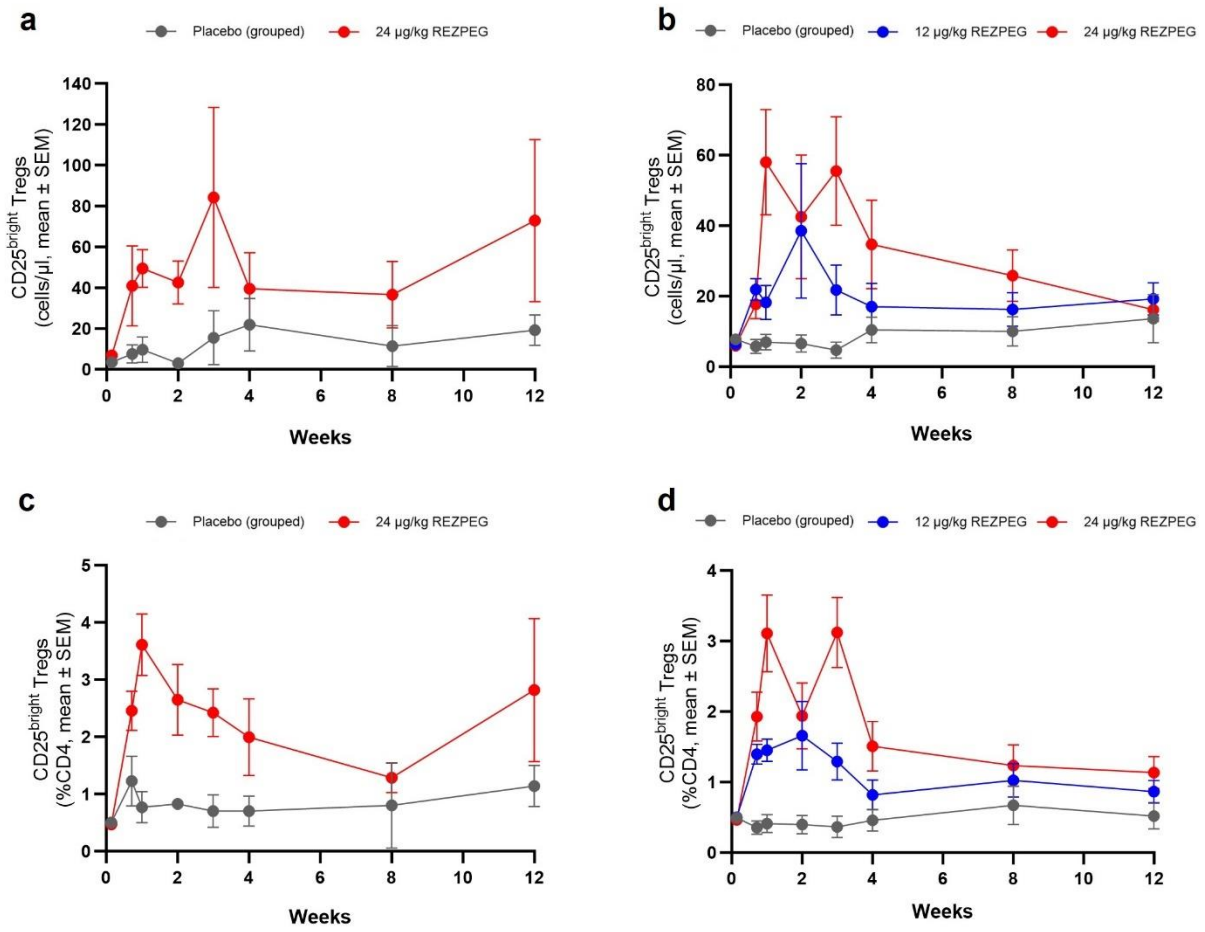
Supplementary Figure 2 | PsO study design and patient completion summary. a, PsO study visits took place at baseline and on days 1, 3, 5, 8, 11, 15, 22, and 29 during the first 4 weeks, then every 2 weeks until the end of the treatment period at week 12, then at weeks 14, 16, and 19 during the off-treatment follow-up period. Week 19 PASI-50 responders were followed during study visits every 4 weeks in an extended follow-up period from weeks 24 to 48. **b**, PsO patient disposition. BSA, body surface area; PASI, psoriasis area and severity index; Q2W, every 2 weeks; PsO, psoriasis; SC, subcutaneously; sPGA, static physician global assessment.

Supplementary Figure 3 | AD study design and patient completion summary



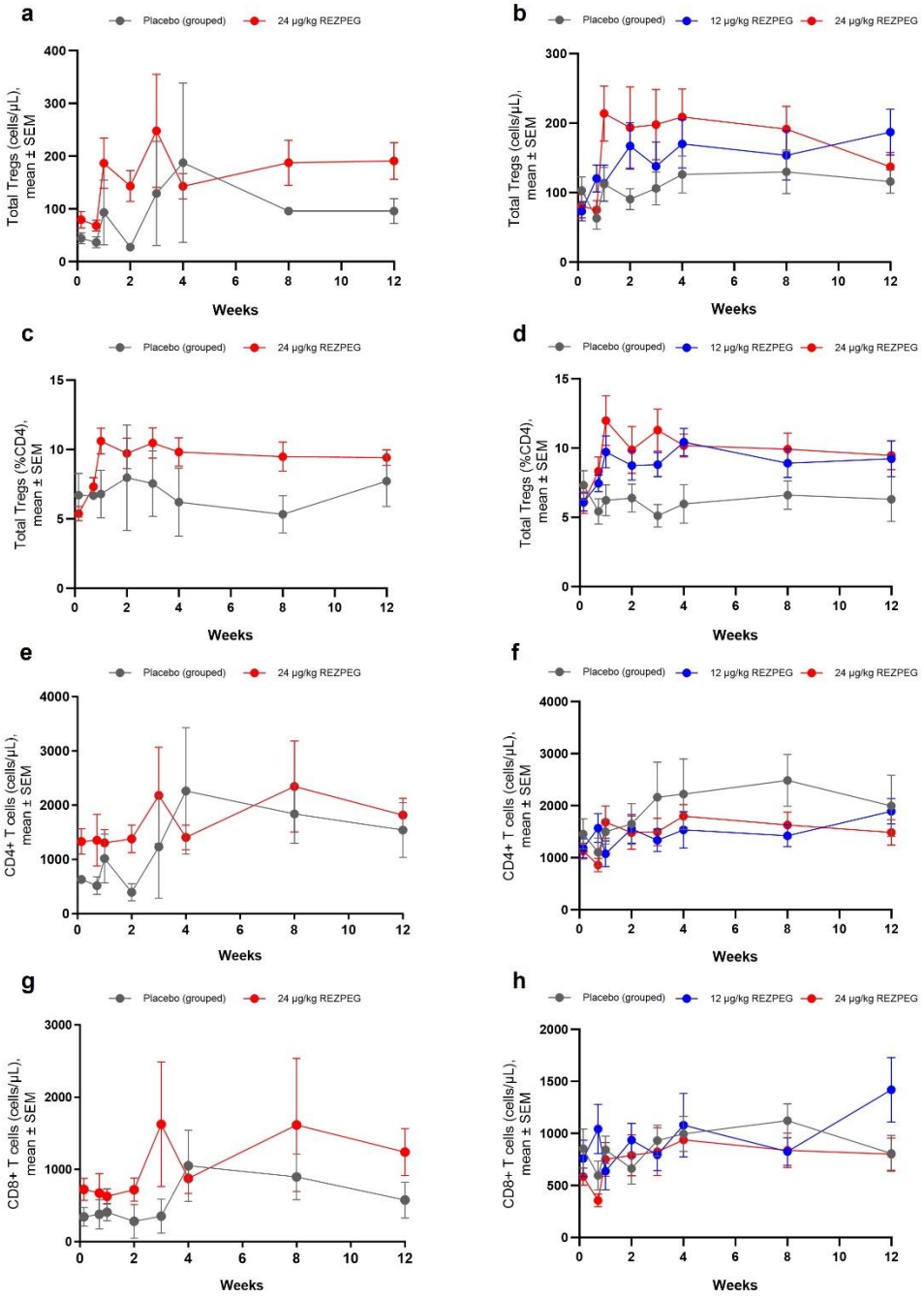
Supplementary Figure 3 | AD study design and patient completion summary. a, AD study visits took place at baseline and on days 1, 3, 5, 8, 11, 15, 22 and 29 during the first 4 weeks, then every two weeks until the end of the treatment period at week 12, then at weeks 14, 16 and 19 during the off-treatment follow-up period. Week 19 EASI-50 responders were followed during study visits every 4 weeks in an extended follow-up period from weeks 24 to 48. **b**, AD patient disposition. AD, atopic dermatitis; BSA, body surface area; EASI, eczema area and severity index; Q2W, every 2 weeks; SC, subcutaneously; vIGA-AD, validated Investigator Global Assessment scale for Atopic Dermatitis.

Supplementary Figure 4 | REZPEG-induced CD25^{bright} Treg pharmacodynamics in PsO and AD patients



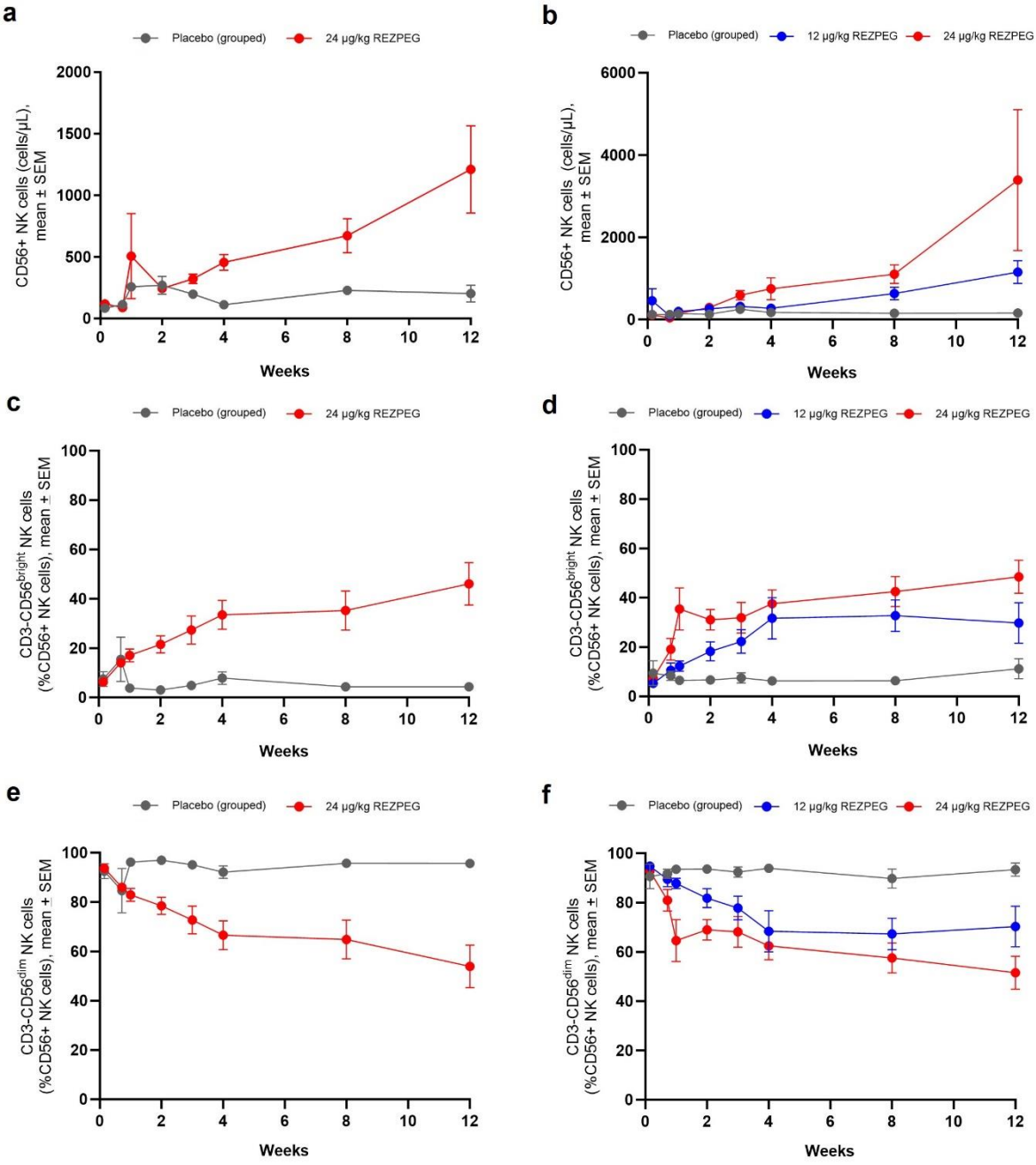
Supplementary Figure 4 | REZPEG-induced CD25^{bright} Treg pharmacodynamics in PsO and AD patients. Total CD25^{bright} Tregs (cells/µL) in **a**, PsO patients and **b**, AD patients. CD25^{bright} Tregs as a percentage of CD4+ T cells in **c**, PsO patients and **d**, AD patients. All measurements performed using peripheral blood samples from patients treated with placebo (grey circles), REZPEG 12 µg/kg (blue circles), or REZPEG 24 µg/kg (red circles) administered once every 2 weeks for 12 weeks. Data shown as mean ± SEM. Number of samples at each time point provided in Supplementary Tables 6 (PsO) and 7 (AD). AD, atopic dermatitis; PsO, psoriasis; SEM, standard error of the mean; Treg, regulatory T cell. Source data are provided as a Source Data file.

Supplementary Figure 5 | REZPEG-induced total Treg and conventional T cell pharmacodynamics in PsO and AD patients



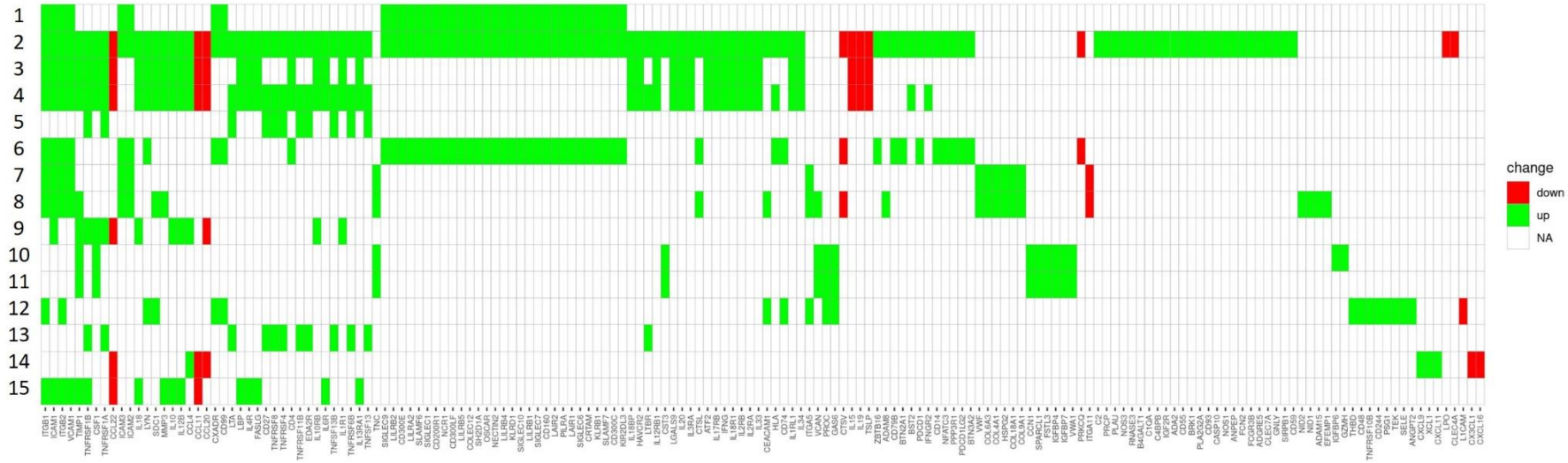
Supplementary Figure 5 | REZPEG-induced Treg and conventional T cell pharmacodynamics in PsO and AD patients. Total Tregs (cells/µL) in **a**, PsO patients and **b**, AD patients. Total Tregs as a percentage of CD4+ T cells in **c**, PsO patients and **d**, AD patients. CD4+ T cells in **e**, PsO and **f**, AD patients. CD8+ T cells in **g**, PsO and **h**, AD patients. All measurements performed using peripheral blood samples from patients treated with placebo (grey circles), REZPEG 12 µg/kg (blue circles), or REZPEG 24 µg/kg (red circles) administered once every 2 weeks for 12 weeks. Data shown as mean ± SEM. Number of samples at each time point provided in Supplementary Tables 6 (PsO) and 7 (AD). AD, atopic dermatitis; PsO, psoriasis; SEM, standard error of the mean; Treg, regulatory T cell. Source data are provided as a Source Data file.

Supplementary Figure 6 | REZPEG NK cell pharmacodynamics in PsO and AD patients



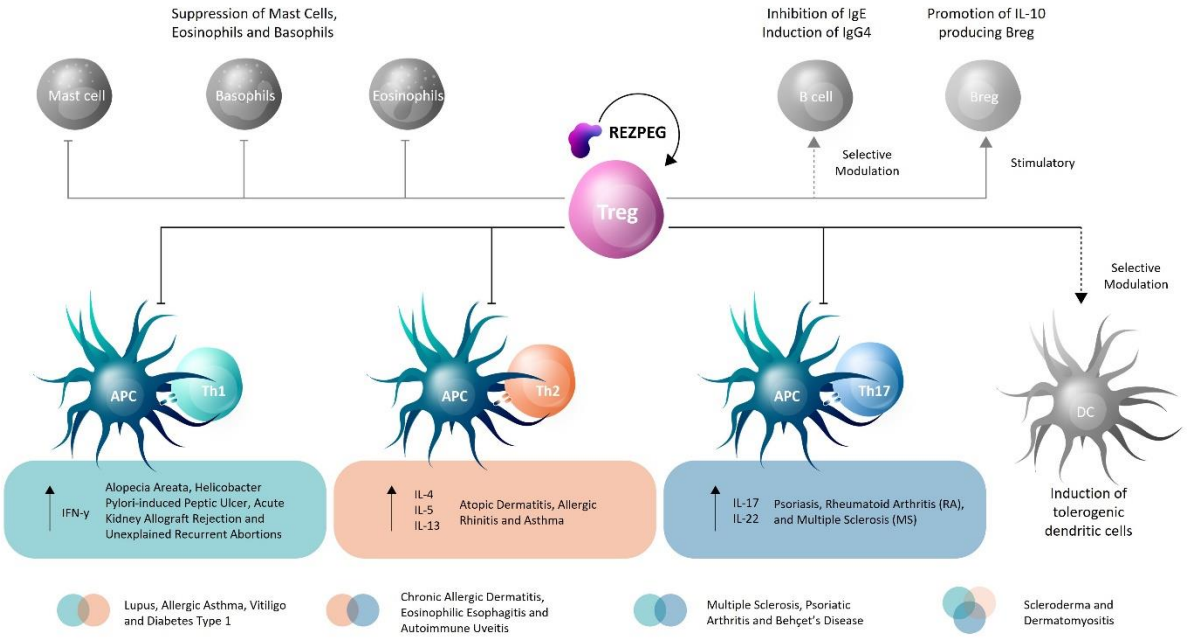
Supplementary Figure 6 | REZPEG NK cell pharmacodynamics in PsO and AD patients. Absolute counts (cells/µL) of total NK cells in **a**, PsO patients and **b**, AD patients. $CD56^{bright}$ NK cells as percentage of CD56+ NK cells in **c**, PsO patients and **d**, AD patients. $CD56^{dim}$ NK cells as a percentage of CD56+ NK cells in **e**, PsO patients and **f**, AD patients. All measurements performed using peripheral blood samples from patients treated with placebo (grey circles), REZPEG 12 µg/kg (blue circles) or 24 µg/kg (red circles) administered once every 2 weeks for 12 weeks. Number of samples at each time point provided in Supplementary Tables 6 (PsO) and 7 (AD). Data shown as mean ± SEM. AD, atopic dermatitis; NK, natural killer; PsO, psoriasis; SEM, standard error of the mean. Source data are provided as a Source Data file.

Supplementary Figure 7 | Serum proteomic pathway analysis



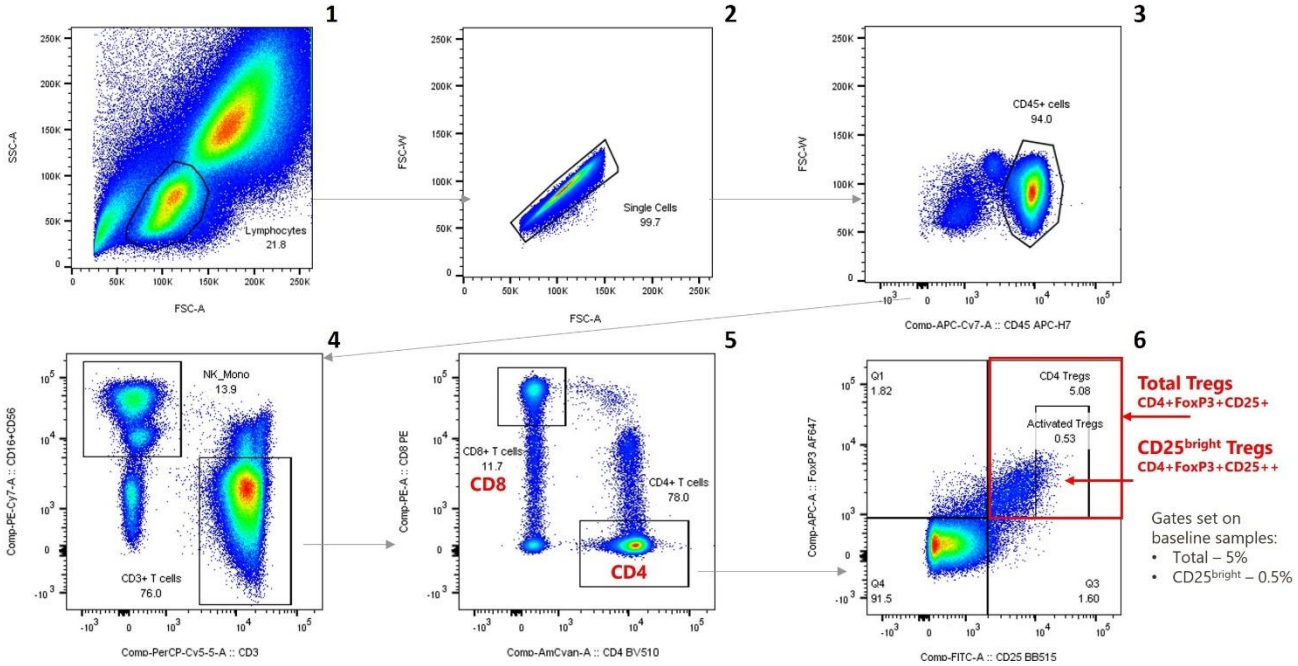
Supplementary Figure 7 | Serum proteomic pathway analysis. Pathway analysis of dose-dependent and statistically significant differences in protein expression in response to REZPEG treatment compared to placebo using the Reactome knowledgebase. Red, downregulated proteins; green, upregulated proteins. Pathways grouped by 1, immunoregulatory interactions between lymphoid and non-lymphoid cells; 2, immune system-related; 3, interleukin signaling; 4, cytokine signaling in the immune system; 5, TNFs binding their physiological receptors; 6, adaptive immune system-related; 7, integrin cell surface interactions; 8, extracellular matrix organization; 9, IL-10 signaling; 10, regulation of insulin-like growth factor transport and uptake by binding proteins; 11, post-translational protein phosphorylation; 12, cell surface interactions at the vascular wall; 13, TNFR2 non-canonical NF-κB pathway; 14, chemokine receptor binding; 15, IL-4 and IL-13 signaling. Number of samples at each time point provided in Supplementary Table 10. IL, interleukin; NA, not applicable; NF-κB, nuclear factor-kappa B; TNF, tumor necrosis factor; TNFR, tumor necrosis factor receptor. Source data are provided as a Source Data file.

Supplementary Figure 8 | REZPEG mechanism of action hypothesis in restoring Treg homeostasis in inflammatory disorders



Supplementary Figure 8 | REZPEG mechanism of action hypothesis in restoring Treg homeostasis in inflammatory disorders. The novel IL-2R pathway agonist REZPEG promotes the proliferation and activation of Tregs that are impaired in diverse pathologies that often involve overlapping immunological pathways. As key immunoregulators, Tregs have a broad range of biological activity, including suppression of APC-driven inflammatory cytokine secretion from Th1, Th2, and Th17 helper T cells. Tregs can also suppress inflammatory mast cells, eosinophils, and basophils. Restoration of immune balance is also achieved by Treg promotion of anti-inflammatory IL-10 production from Bregs, selective modulation of B cells by inhibition of IgE or induction of IgG4, or via induction of tolerogenic dendritic cells. APC, antigen presenting cell; Breg, regulatory B cell; DC, dendritic cell; IFN-γ, interferon gamma; IgG4, immunoglobulin G4; IgE, immunoglobulin E; IL-2R, interleukin-2 receptor; Treg, regulatory T cell.

Supplementary Figure 9 | Example gating strategy for CD25^{bright} Treg flow cytometry immunophenotyping



Supplementary Figure 9 | Example gating strategy for CD25^{bright} Treg flow cytometric immunophenotyping. Gating was performed as reported in Fanton et al, 2022. Briefly, after gating on lymphocytes (box 1), positive populations were identified based on fluorescence minus one control. Total Tregs were defined as CD45+CD3+CD4+CD25+FoxP3+ (box 6); CD25^{bright} Tregs were defined as CD45+CD3+CD4+CD25++FoxP3+ (box 6); CD4+ T cells as CD45+CD3+CD4+ (box 5); CD8+ T cells as CD45+CD3+CD8+ (box 5); and total NK cells as CD45+CD3-CD56+ (box 4). NK cells were further phenotyped from the CD3-CD56+ population in box 4 as CD56^{bright} and CD56^{dim}. To ensure comparability across longitudinal samples, the baseline total Treg gate was set to approximately 5% (4-6%) of CD4+ T cells for each individual, and this gate position was maintained across the individual's timepoints. For CD25^{bright} Tregs, the baseline gate was set at approximately 0.5% (0.4-0.6%) of CD4+ T cells for each individual. FOXP3, forkhead box protein P3; FSC-W, forward light scatter width; NK, natural killer; SSC-A, side scatter parameter; Treg, regulatory T cell.

Supplementary Table 1 | REZPEG exposure in AD and PsO patients: Estimated C_{max} and AUC_{last}

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	Dose (µg/kg)	C_{max} (ng/mL)	AUC_{last} (ng*day/mL)
AD	12	102.01	1144.93
	24	218.68	2146.91
PSO	24	192.64	1841.04

AD, atopic dermatitis; AUC_{last}, area under the curve from dosing to the time of the last measured concentration; C_{max}, geometric mean maximum concentration; PsO, psoriasis.

Supplementary Table 2 | REZPEG efficacy in PsO patients at week 12

Supplementary Table 2 | Week 12 PsO efficacy measures

	n	Placebo	24 µg/kg REZPEG
Target lesion TSS % change from baseline (SEM)	5, 11	-1.1 (13.9)	-51.0 (9.0)
Treatment difference (95% CI)		---	-49.9 (-82.8, -16.9)
P value			0.004
BSA % change from baseline (SEM)	5, 11	-8.6 (19.3)	-29.4 (12.3)
Treatment difference (95% CI)		---	-20.7 (-66.5, 25.0)
P value			0.369
PASI % change from baseline (SEM)	5, 11	-26.2 (12.9)	-44.5 (8.3)
Treatment difference (95% CI)		---	-18.3 (-49.1, 12.4)
P value			0.239
Itch NRS % change from baseline (SEM)	5, 11	-3.1 (19.4)	-40.3 (12.7)
Treatment difference (95% CI)		---	-37.2 (-83.4, 9.0)
P value			0.113
PGA % change from baseline (SEM)	5, 11	8.4 (15.3)	-27.4 (10.2)
Treatment difference (95% CI)		---	-35.8 (-72.3, 0.8)
P value			0.055

A mixed model for repeated measures (MMRM) was used to generate Least-Squares Means for percent change from baseline in continuous efficacy variables with baseline score as the covariate, treatment arm and protocol-defined visit time and their interaction as the fixed factors. Visit time is also used as repeated measure to account for within-subject variability. Differences and their P values were derived for treatment vs placebo based on Least-Squares Means. 10 ug/kg REZPEG data were not presented due to small sample size. All analyses were based on the adjusted ITT population. BSA, body surface area; ITT, intent-to-treat; NRS, numerical rating scale; PASI, psoriasis area and severity index; PGA, Patient's Global Assessment of Disease Severity; SEM, standard error of the mean; TSS, Total Sign Score.

Supplementary Table 3 | Efficacy durability in AD REZPEG 24 µg/kg cohort

Supplementary Table 3 | Efficacy durability in REZPEG 24 µg/kg cohort

	Responders at EOT	Responders 7 wk after EOT	Responders 36 wk after EOT	% Durability between wk 12 and wk 48
	Week 12	**Week 19**	**Week 48**	
EASI-50	12	10	7	58.33
EASI-75	7	9	5	71.43
EASI-90	4	5	4	100.0
vIGA[a]	5	6	4	80.00
Itch NRS[b]	7	7	5	71.43
POEM[c]	11	11	7	63.64
DLQI[d]	12	10	5	41.67

BSA; body surface area; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; EASI-50, patients with a 50% decrease in EASI score from baseline; EASI-75, patients with a 75% decrease in EASI score from baseline; EASI-90, patients with a 90% decrease in EASI score from baseline; EOT, end-of-treatment at 12 weeks; NRS, numeric rating scale; POEM, Patient-Oriented Eczema Measure; vIGA-AD, Validated Investigator Global Assessment for Atopic Dermatitis. [a] Patients with post-baseline vIGA-AD scores of 0 or 1, with ≥ 2-point improvement from baseline. [b] Proportion with post-baseline itch scale reduced by ≥ 4 points among patients with baseline score ≥ 4. [c] Proportion with post-baseline POEM score reduced by ≥ 4 points among patients with baseline score ≥ 4. [d] Proportion with post-baseline DLQI score reduced by ≥ 4 points among patients with baseline score ≥ 4.

Supplementary Table 4 | Table of statistically significant and list of non-significant serum proteomic biomarkers

Assay	OlinkID	UniProt	*P* Value 24 µg/kg vs. placebo	*P* Value 12 µg/kg vs. placebo
NCR1	OID20566	O76036	< 1.00E-15	< 1.00E-15
CD160	OID20647	O95971	< 1.00E-15	1.02E-14
FASLG	OID20665	P48023	< 1.00E-15	8.18E-14
KLRB1	OID20629	Q12918	< 1.00E-15	9.66E-14
KLRD1	OID20632	Q13241	< 1.00E-15	1.14E-12
XCL1	OID21398	P47992	< 1.00E-15	6.42E-12
CXCL16	OID20282	Q9H2A7	< 1.00E-15	5.45E-10
CD163	OID20360	Q86VB7	< 1.00E-15	3.85E-09
IL2RA	OID20267	P01589	< 1.00E-15	9.61E-09
CD244	OID20628	Q9BZW8	< 1.00E-15	1.11E-08
IL15	OID20562	P40933	< 1.00E-15	2.42E-07
GZMA	OID20663	P12544	< 1.00E-15	0.003
LILRB2	OID20301	Q8N423	5.33E-15	6.80E-06
GNLY	OID21132	P22749	5.77E-15	4.39E-06
SIGLEC7	OID20190	Q9Y286	9.66E-15	2.39E-05
IL10	OID20431	P22301	2.24E-14	2.99E-04
LY9	OID20670	Q9HBG7	3.46E-14	6.88E-09
ADGRG1	OID21294	Q9Y653	5.55E-14	1.90E-12
LTA	OID20586	P01374	5.92E-14	9.69E-06
CD300C	OID21010	Q08708	1.25E-13	2.66E-07
ICAM1	OID20411	P05362	3.00E-13	6.73E-07
LAIR1	OID20737	Q6GTX8	6.52E-12	1.17E-05
SIGLEC1	OID20690	Q9BZZ2	8.54E-12	7.27E-08
SLAMF8	OID21214	Q9P0V8	9.76E-12	4.63E-05
IL2RB	OID20450	P14784	1.79E-11	5.53E-04
CCL23	OID20693	P55773	1.87E-11	2.63E-06
MARCO	OID20210	Q9UEW3	1.97E-11	3.01E-05
IL12RB1	OID20486	P42701	4.90E-11	2.81E-08
ITGB2	OID20315	P05107	7.15E-11	4.72E-04
KIR2DL3	OID21196	P43628	8.81E-11	7.33E-06
CSF1	OID20719	P09603	1.03E-10	5.44E-07
VSIG4	OID21144	Q9Y279	1.52E-10	0.007
CRTAM	OID20914	O95727	1.93E-10	5.69E-05
TNFRSF1B	OID21145	P20333	2.28E-10	2.18E-06
DLL1	OID21525	O00548	3.48E-10	3.76E-06
ADA2	OID20394	Q9NZK5	4.04E-10	2.77E-04
LBP	OID20355	P18428	7.20E-10	4.19E-07
MSR1	OID21063	P21757	1.59E-09	0.038
CRHBP	OID20747	P24387	2.35E-09	7.26E-04
CEACAM21	OID20548	Q3KPI0	2.98E-09	1.47E-05
ENPP2	OID20288	Q13822	3.40E-09	0.002
CD83	OID20565	Q01151	4.65E-09	6.93E-04
B4GALT1	OID20780	P15291	4.91E-09	4.76E-09
CD48	OID20692	P09326	6.89E-09	1.66E-04
SIGLEC10	OID20537	Q96LC7	7.47E-09	3.92E-04
LILRB1	OID20323	Q8NHL6	7.80E-09	NA
HAVCR2	OID21137	Q8TDQ0	1.06E-08	1.25E-04
CTSL	OID20228	P07711	1.21E-08	5.86E-04
IL12A, IL12B	OID21327	P29459, P29460	1.29E-08	0.005
FCRL6	OID20529	Q6DN72	1.70E-08	1.03E-06
VCAM1	OID20396	P19320	2.62E-08	2.30E-05
SLAMF6	OID21254	Q96DU3	2.75E-08	0.001
IL18R1	OID20652	Q13478	3.41E-08	0.006
LILRA2	OID21152	Q8N149	3.99E-08	6.03E-04
IL12B	OID20666	P29460	7.75E-08	0.034
SH2D1A	OID20514	O60880	1.54E-07	NA
IGFBP7	OID20236	Q16270	1.56E-07	NA
ANGPT2	OID21463	O15123	2.87E-07	0.001
TIMD4	OID20375	Q96H15	3.06E-07	NA
NRP1	OID20390	O14786	3.21E-07	3.72E-07
CD300LF	OID21469	Q8TDQ1	6.91E-07	NA
SIRPB1	OID20739	O00241	8.24E-07	0.002
CCL14	OID20401	O16627	8.61E-07	1.34E-04
CD27	OID21527	P26842	9.16E-07	0.003
CCL24	OID20772	O00175	9.66E-07	NA
IL1RL1	OID20250	Q01638	1.07E-06	NA
AXL	OID20363	P30530	1.36E-06	0.003
COL18A1	OID20332	P39060	1.52E-06	3.18E-04
PRCP	OID20337	P42785	1.77E-06	0.015
CCL18	OID20395	P55774	1.90E-06	0.024
CA6	OID21096	P23280	1.96E-06	0.016
FCN2	OID20382	O15485	2.25E-06	0.002
C1QA	OID20654	P02745	2.38E-06	NA
NID1	OID20362	P14543	2.95E-06	1.51E-04
TNC	OID20359	P24821	2.97E-06	NA
DSC2	OID21079	Q02487	3.02E-06	0.016
ICAM3	OID20277	P32942	3.30E-06	NA
BST2	OID21029	Q10589	4.89E-06	0.002
IL18	OID20694	Q14116	4.97E-06	0.013
ITM2A	OID20504	O43736	5.33E-06	0.011
COL4A1	OID20208	P02462	6.80E-06	0.035
CPVL	OID21435	Q9H3G5	6.83E-06	1.12E-04
NOS1	OID20863	P29475	6.93E-06	0.001
TMPRSS5	OID20947	Q9H3S3	7.72E-06	NA
ANGPTL3	OID20407	Q9Y5C1	8.54E-06	NA
GZMB	OID20604	P10144	8.61E-06	NA
ADGRE2	OID20755	Q9UHX3	9.04E-06	1.07E-04
OSCAR	OID20776	Q8IYS5	1.03E-05	0.018
TACSTD2	OID21447	P09758	1.05E-05	0.001
CLC	OID20126	Q05315	1.42E-05	0.005
ALDH3A1	OID20512	P30838	1.55E-05	0.016
FCGR3B	OID20387	O75015	1.56E-05	0.028
THBS4	OID20368	P35443	1.67E-05	1.24E-07
KCNIP4	OID20813	Q6PIL6	1.84E-05	0.001
C4BPB	OID21481	P20851	1.99E-05	0.004
CD79B	OID20635	P40259	2.26E-05	0.003
LGALS7_LGALS7B	OID21406	P47929	2.48E-05	0.007
SEMA7A	OID20283	O75326	3.07E-05	7.86E-05
ADGRE5	OID20260	P48960	3.42E-05	0.001
PBLD	OID20839	P30039	4.51E-05	NA
ITGA5	OID21139	P08648	4.52E-05	NA
ENPP7	OID20689	Q6UWV6	4.58E-05	4.40E-06
CD300E	OID21418	Q496F6	4.97E-05	9.93E-05
GFRA1	OID21457	P56159	5.19E-05	NA
PILRA	OID21129	Q9UKJ1	5.71E-05	0.002
CD74	OID21040	P04233	6.06E-05	0.004
IL20	OID20453	Q9NYY1	8.42E-05	NA
LGALS9	OID20781	O00182	8.82E-05	0.002
ADAM15	OID20109	Q13444	9.54E-05	4.82E-06
WARS	OID21084	P23381	9.54E-05	0.005
CLEC7A	OID20636	Q9BXN2	9.63E-05	NA
CDH5	OID20243	P33151	9.77E-05	6.87E-05
HSPG2	OID20383	P98160	9.78E-05	5.25E-05
NOTCH1	OID20311	P46531	9.86E-05	0.023
DRAXIN	OID20917	Q8NBI3	1.03E-04	0.024
HLA_DRA	OID20520	P01903	1.06E-04	NA
IL34	OID20809	Q6ZMJ4	1.16E-04	0.001
TIMP1	OID20418	P01033	1.20E-04	4.25E-04
ASAH2	OID20996	Q9NR71	1.51E-04	NA
WFIKKN1	OID20939	Q96NZ8	1.53E-04	0.003
LILRB4	OID20429	Q8NHJ6	1.62E-04	0.004
LILRB5	OID20324	O75023	1.73E-04	NA
KEL	OID20881	P23276	1.76E-04	0.001
CST3	OID20400	P01034	1.80E-04	2.83E-04
IL10RB	OID20696	Q08334	2.12E-04	8.06E-05
RNASE3	OID20203	P12724	2.15E-04	NA
DSG3	OID21460	P32926	2.17E-04	0.001
LPO	OID20963	P22079	2.19E-04	0.046
AGR2	OID20896	O95994	2.23E-04	1.55E-05
SDC1	OID20169	P18827	2.24E-04	0.028
TNFRSF1A	OID21155	P19438	2.28E-04	0.003
VCAN	OID21026	P13611	2.44E-04	0.023
ADAM8	OID21039	P78325	2.63E-04	NA
TNFSF13B	OID20272	Q9Y275	2.70E-04	0.001
TNFSF13	OID20733	O75888	3.07E-04	0.005
IL33	OID20428	O95760	3.30E-04	0.012
SERPINA9	OID21284	Q86WD7	3.32E-04	NA
TDGF1	OID20816	P13385	4.29E-04	4.20E-05
SEMA4D	OID21020	Q92854	4.36E-04	0.034
ACP5	OID20314	P13686	4.45E-04	NA
IL18BP	OID20348	O95998	4.46E-04	0.010
MZB1	OID20732	Q8WU39	4.58E-04	0.011
KITLG	OID20196	P21583	4.65E-04	NA
ATF2	OID20798	P15336	4.76E-04	NA
THBD	OID20231	P07204	5.04E-04	NA
RRM2	OID21187	P31350	5.30E-04	NA
LAIR2	OID20965	Q6ISS4	5.63E-04	0.006
LSM1	OID21210	O15116	6.38E-04	7.26E-07
IL6R	OID20385	P08887	6.48E-04	0.003
FLT4	OID21491	P35916	6.81E-04	0.003
SCARB2	OID20943	Q14108	7.07E-04	3.14E-04
C19orf12	OID20804	Q9NSK7	7.17E-04	NA
SLAMF7	OID20602	Q9NQ25	7.30E-04	0.001
CD59	OID20339	P13987	7.88E-04	NA
CD200R1	OID20595	Q8TD46	8.02E-04	0.030
CDCP1	OID20940	Q9H5V8	8.59E-04	0.010
IL17RB	OID20585	Q9NRM6	8.84E-04	0.013
LAP3	OID20436	P28838	9.10E-04	0.012
EPO	OID20522	P01588	9.77E-04	NA
VWF	OID20256	P04275	0.001	NA
KRT5	OID20860	P13647	0.001	0.049
SIGLEC6	OID21394	O43699	0.001	4.61E-04
TNFRSF8	OID21049	P28908	0.001	NA
DCXR	OID21480	Q7Z4W1	0.001	NA
CCL22	OID20765	O00626	0.001	0.003
KLK8	OID21517	O60259	0.001	NA
CLEC4A	OID20573	Q9UMR7	0.001	0.020
SIGLEC9	OID21390	Q9Y336	0.001	NA
CXCL9	OID20675	Q07325	0.001	NA
CTSV	OID21405	O60911	0.001	NA
COL6A3	OID20292	P12111	0.001	0.028
GRPEL1	OID21309	Q9HAV7	0.001	0.009
CD6	OID20649	P30203	0.001	NA
TPPP3	OID20842	Q9BW30	0.001	NA
THY1	OID21050	P04216	0.002	0.003
BRK1	OID20883	Q8WUW1	0.002	0.046
FSTL3	OID20782	O95633	0.002	0.006
CST5	OID20995	P28325	0.002	NA
CCL26	OID20546	Q9Y258	0.002	NA
CD93	OID20397	Q9NPY3	0.002	0.002
C2	OID20410	P06681	0.002	4.17E-04
FCRL3	OID20443	Q96P31	0.002	0.003
AGXT	OID20139	P21549	0.002	NA
BTN2A1	OID20713	Q7KYR7	0.002	0.001
ITGA11	OID20581	Q9UKX5	0.002	NA
PLA2G7	OID21105	Q13093	0.002	NA
CX3CL1	OID20976	P78423	0.002	NA
TINAGL1	OID20180	Q9GZM7	0.002	NA
PLA2G2A	OID20274	P14555	0.002	NA
GDF15	OID20251	Q99988	0.002	3.48E-04
NTproBNP	OID20125	NTproBNP	0.002	0.036
ICAM2	OID20248	P13598	0.002	NA
MET	OID20269	P08581	0.002	0.030
CA5A	OID20075	P35218	0.002	NA
RARRES2	OID20373	Q99969	0.002	0.002
MMP3	OID21083	P08254	0.002	NA
NOS3	OID20834	P29474	0.002	NA
RBP5	OID21369	P82980	0.003	0.010
NID2	OID21085	Q14112	0.003	0.022
CD4	OID20584	P01730	0.003	0.030
FGF21	OID21402	Q9NSA1	0.003	NA
CRIM1	OID20701	Q9NZV1	0.003	0.010
HTRA2	OID21471	O43464	0.003	0.006
TNFRSF10B	OID20981	O14763	0.003	6.82E-05
HYOU1	OID20300	Q9Y4L1	0.003	NA
CD38	OID21316	P28907	0.003	NA
IFNG	OID20495	P01579	0.003	4.49E-04
HAO1	OID21395	Q9UJM8	0.003	NA
ADA	OID20645	P00813	0.004	NA
PDCD1	OID21396	Q15116	0.004	NA
IL1R1	OID21116	P14778	0.004	NA
TNFRSF21	OID21052	O75509	0.004	NA
LTBR	OID20768	P36941	0.004	1.38E-04
PDCD1LG2	OID21273	Q9BQ51	0.005	0.003
IGF2R	OID21146	P11717	0.005	NA
SPARCL1	OID20361	Q14515	0.005	0.020
ITIH3	OID20352	Q06033	0.005	NA
GFRA3	OID20933	O60609	0.005	NA
GOLM2	OID21044	Q6P4E1	0.005	NA
IL4R	OID20576	P24394	0.005	0.001
SPON2	OID20221	Q9BUD6	0.005	NA
EDA2R	OID21451	Q9HAV5	0.005	1.64E-04
AIFM1	OID21287	O95831	0.005	NA
TFPI2	OID21512	P48307	0.005	NA
IGFBP6	OID20413	P24592	0.006	0.007
PPP3R1	OID20902	P63098	0.006	NA
PTPRM	OID20598	P28827	0.007	1.42E-04
IGFBP4	OID21158	P22692	0.007	8.52E-07
FGFBP1	OID21507	Q14512	0.007	0.014
PLAU	OID21124	P00749	0.007	NA
GAS6	OID20318	Q14393	0.007	NA
MATN2	OID20767	O00339	0.007	NA
CD14	OID20378	P08571	0.007	0.006
TGFBI	OID20417	Q15582	0.008	0.032
NOMO1	OID21106	Q15155	0.008	0.008
ART3	OID20346	Q13508	0.008	0.003
ROBO2	OID21007	Q9HCK4	0.008	NA
PPY	OID21516	P01298	0.008	0.037
LAMP3	OID20638	Q9UQV4	0.008	0.036
PLXNB2	OID20317	O15031	0.008	0.026
ZBTB16	OID21205	Q05516	0.009	NA
PTS	OID20847	Q03393	0.009	NA
IL13RA1	OID21504	P78552	0.009	0.020
PGF	OID20673	P49763	0.009	NA
GZMH	OID20096	P20718	0.009	NA
CCL20	OID20671	P78556	0.009	0.005
TSLP	OID20056	Q969D9	0.010	0.002
ANGPTL2	OID20726	Q9UKU9	0.010	NA
CNTNAP2	OID20556	Q9UHC6	0.010	0.002
TNFRSF4	OID20653	P43489	0.011	NA
USO1	OID21367	O60763	0.011	0.005
CCN1	OID21368	O00622	0.011	0.015
CEACAM1	OID21528	P13688	0.011	0.000
EPHB4	OID20242	P54760	0.011	0.036
ANG	OID20403	P03950	0.013	3.09E-04
EFNA1	OID21125	P20827	0.013	0.004
FST	OID20770	P19883	0.013	0.031
ANXA5	OID20810	P08758	0.014	0.018
COLEC12	OID20738	Q5KU26	0.014	0.000
CD302	OID21328	Q8IX05	0.014	0.022
NECTIN2	OID20222	Q92692	0.014	0.003
TEK	OID21496	Q02763	0.016	0.011
HS3ST3B1	OID21303	Q9Y662	0.016	0.004
BTN3A2	OID20540	P78410	0.017	0.025
CD109	OID21108	Q6YHK3	0.017	NA
TNFRSF6B	OID20964	O95407	0.018	NA
CASP10	OID20893	Q92851	0.018	NA
AKR1C4	OID20062	P17516	0.021	2.96E-04
SELE	OID20290	P16581	0.022	NA
ACOX1	OID20124	Q15067	0.022	0.012
WFDC2	OID21505	Q14508	0.023	0.011
XPNPEP2	OID21508	O43895	0.023	NA
CXCL11	OID21042	O14625	0.023	0.001
LYN	OID21350	P07948	0.025	0.008
PRKCQ	OID20468	Q04759	0.026	NA
FAM3C	OID20233	Q92520	0.027	0.011
L1CAM	OID21484	P32004	0.029	NA
NAMPT	OID21227	P43490	0.035	0.008
CLSTN2	OID20664	Q9H4D0	0.036	NA
CCL4	OID20695	P13236	0.039	0.011
ITGB1	OID20376	P05556	0.039	0.006
VEGFD	OID20662	O43915	0.040	NA
APOM	OID20374	O95445	0.040	NA
PRSS8	OID20763	Q16651	0.040	NA
MANSC1	OID21492	Q9H8J5	0.041	0.005
EFNA4	OID20935	P52798	0.047	0.005
EBI3_IL27	OID21389	Q14213_Q8NEV9	0.050	0.005
CCL11	OID20668	P51671	0.050	0.004
CALB2	OID20801	P22676	NA	1.32E-06
REG1B	OID20266	P48304	NA	0.001
CXCL14	OID20458	O95715	NA	0.001
OXT	OID21047	P01178	NA	0.001
IL19	OID20158	Q9UHD0	NA	0.001
VWA1	OID21421	Q6PCB0	NA	0.002
TNFRSF11B	OID20735	O00300	NA	0.002
VASN	OID20345	Q6EMK4	NA	0.003
WNT9A	OID20460	O14904	NA	0.003
CD55	OID20377	P08174	NA	0.003
HSPB6	OID21408	O14558	NA	0.004
NXPH1	OID20849	P58417	NA	0.004
PSPN	OID20511	O60542	NA	0.004
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MDK	OID21489	P21741	NA	0.004
EFEMP1	OID20414	Q12805	NA	0.004
PSG1	OID20916	P11464	NA	0.004
CD276	OID20680	Q5ZPR3	NA	0.005
RSPO3	OID21415	Q9BXY4	NA	0.005
GCNT1	OID21379	Q02742	NA	0.005
SMOC2	OID20730	Q9H3U7	NA	0.005
ANPEP	OID20350	P15144	NA	0.005
CD99	OID21110	P14209	NA	0.006
PROC	OID20402	P04070	NA	0.006
FABP4	OID20245	P15090	NA	0.006
PCDH17	OID20132	O14917	NA	0.006
SCARF2	OID21048	Q96GP6	NA	0.006
TGFBR2	OID21493	P37173	NA	0.007
IL3RA	OID20461	P26951	NA	0.009
SSC5D	OID20351	A1L4H1	NA	0.009
CLSTN1	OID20874	O94985	NA	0.009
NFATC3	OID20470	Q12968	NA	0.009
CXADR	OID20561	P78310	NA	0.010
CALB1	OID21306	P05937	NA	0.018
IFNGR2	OID20941	P38484	NA	0.019
ERBB4	OID21510	Q15303	NA	0.019
SNCG	OID20971	O76070	NA	0.026
CHRDL2	OID20223	Q6WN34	NA	0.032
FOLR1	OID21529	P15328	NA	0.041
COL9A1	OID20550	P20849	NA	0.046

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, PSRC1, PTEN, PTGDS, PTH1R, PTK7, PTN, PTPN1, PTPN6, PTPRF, PTPRN2, PTPRS, P
TX3, PVALB, PVR, PXN, QDPR, QPCT, RAB37, RAB6A, RAB6B, RABEPK, RABGAP1L, RAD2
3B, RANGAP1, RARRES1, RASA1, RASSF2, RBKS, RBP2, RCOR1, REG1A, REG3A, REG4, R
ELT, REN, RET, RETN, RGMA, RGMB, RGS8, RHOC, RILP, RNASET2, RNF41, ROBO1, ROR
1, RP2, RRM2B, RSPO1, RTBDN, RTN4R, RUVBL1, RWDD1, S100A11, S100A12, S100A16,
S100A4, S100P, SAMD9L, SCAMP3, SCARA5, SCARB1, SCARF1, SCG2, SCG3, SCGB1A1, S
CGB3A2, SCGN, SCLY, SCP2, SCRN1, SDC4, SELP, SELPLG, SEMA3F, SEMA4C, SEPTIN9,
SERPINA11, SERPINA12, SERPINB1, SERPINB5, SERPINB6, SERPINB8, SERPINB9, SERPI
NE1, SESTD1, SETMAR, SEZ6L, SEZ6L2, SF3B4, SFRP1, SFTPA1, SFTPA2, SFTPD, SH2B
3, SHMT1, SIAE, SIGLEC15, SIGLEC5, SIRPA, SIRT2, SIRT5, SIT1, SKAP1, SKAP2, S
LAMF1, SLC16A1, SLC27A4, SLC39A14, SLC39A5, SLIT2, SLITRK2, SLITRK6, SMAD5, S
MARCA2, SMOC1, SMPD1, SMPDL3A, SNAP23, SNAP29, SNX9, SOD1, SOD2, SORCS2, SORD
, SORT1, SOST, SPARC, SPINK1, SPINK4, SPINK5, SPINK6, SPINT1, SPINT2, SPOCK1,
SPON1, SPP1, SPRY2, SRC, SRP14, SRPK2, SSB, SSC4D, ST3GAL1, ST6GAL1, STAMBP,
STAT5B, STC1, STC2, STIP1, STK11, STK24, STK4, STX16, STX4, STX6, STX8, STXBP
3, SUGT1, SULT1A1, SULT2A1, SUMF2, SUSD1, SUSD2, TACC3, TAFA5, TANK, TARBP2,
TBC1D17, TBC1D23, TBC1D5, TBCB, TBCC, TBL1X, TCL1A, TCL1B, TCN2, TDRKH, TFF1,
TFF2, TFF3, TFPI, TFRC, TGFA, TGFB1, TGFBR3, TGM2, THBS2, THOP1, THPO, TIA1,
TIE1, TIGAR, TIMP3, TIMP4, TJAP1, TLR3, TMPRSS15, TMSB10, TNF, TNFAIP8, TNFRS
F10A, TNFRSF10C, TNFRSF11A, TNFRSF12A, TNFRSF13B, TNFRSF13C, TNFRSF14, TNFRSF
19, TNFRSF9, TNFSF10, TNFSF11, TNFSF12, TNFSF14, TNNI3, TNR, TNXB, TP53, TP53
INP1, TPMT, TPP1, TPSAB1, TPT1, TRAF2, TREM2, TREML2, TRIAP1, TRIM21, TRIM5,
TSHB, TSPAN1, TST, TXLNA, TXNDC15, TXNDC5, TXNRD1, TYMP, TYRO3, UBAC1, ULBP2,
UMOD, USP8, UXS1, VAMP5, VASH1, VAT1, VEGFA, VEGFC, VIM, VMO1, VNN2, VPS37A,
VPS53, VSIR, VSTM1, VSTM2L, VTA1, VTCN1, VWC2, WAS, WASF1, WASF3, WFDC12, WFI
KKN2, WIF1, WWP2, XG, XRCC4, YES1, YTHDF3, ZBTB17

Supplementary Table 4 | Table of statistically significant and list of non-significant serum proteomic biomarkers. Differentially-detected serum proteins in AD patients over the 12-week REZPEG treatment induction period compared to placebo using Olink Explore panels. Data were fitted with a linear mixed model with multiple testing correction using Benjamini-Hochberg. Statistical comparisons were made between treatment and placebo using the Tukey method. Proteins with a statistically significant treatment-based change (threshold $p < 0.05$) are shown in the table. Proteins that were not significantly different are listed below the table. Number of samples evaluated at each time point are provided in Supplementary Table 10. Source data are provided as a Source Data file.

Supplementary Table 5 | Table of statistically significant REZPEG-modulated proteins grouped by pathway

	gs_exact_source	gs_description, pathway name	p value	# found in pathway	total in pathway	genes/proteins_up	genes/proteins_down
1	R-HSA-198933	Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell	1.11E-16	37	249	SIGLEC9, LILRB2, ITGB1, CD300E, LILRA2, ICAM3, SLAMF6, SIGLEC1, ICAM1, CD200R1, NCR1, CD300LF, LILRB5, COLEC12, SH2D1A, OSCAR, NECTIN2, LILRB4, KLRD1, CXADR, SIGLEC10, LILRB1, VCAM1, SIGLEC7, CD160, LAIR2, PILRA, LAIR1, SIGLEC6, CD99, CRTAM, KLRB1, ICAM2, ITGB2, SLAMF7, CD300C, KIR2DL3	
2	R-HSA-168256	Immune System	1.11E-16	136	2627	LILRB2, SLAMF6, IL18BP, IL18, LYN, C2, CD300LF, HAVCR2, LTA, PRCP, LTBR, ZBTB16, PLAU, SH2D1A, LBP, IL12RB1, TIMP1, ADAM8, LILRB4, CST3, SIGLEC9, SIGLEC10, NOS3, IL4R, CSF1, RNASE3, FASLG, SDC1, B4GALT1, ICAM1, CD27, CD79B, LGALS9, BTN2A1, TNFRSF8, IL20, TNFRSF4, CD160, C1QA, C4BPB, IL3RA, IGF2R, ADA2, CD55, BRK1, PLA2G2A, CD4, CD200R1, VCAM1, ICAM3, CTSL, PILRA, CD93, BST2, TNFRSF1A, ITGB2, PDCD1, ATF2, CD300C, CASP10, NOS1, IFNGR2, IL17RB, LILRB5, CRTAM, MMP3, SIGLEC6, IL10, CD300E, ANPEP, IFNG, IL18R1, FCN2, FCGR3B, ADGRE5, TNFRSF11B, EDA2R, IL2RB, NECTIN2, KLRD1, SIGLEC1, IL2RA, IL10RB, CLEC7A, IL6R, TNFSF13B, IL12B, OSCAR, TNFRSF1B, LAIR2, IL33, LILRA2, SIGLEC7, LAIR1, CD99, ICAM2, CCL4, KLRB1, KIR2DL3, GNLY, IL1R1, CD14, CEACAM1, TNFRSF6B, HLA_DRA, NCR1, NFATC3, CD74, PPP3R1, PDCD1LG2, BTN3A2, SIRPB1, SLAMF7, ITGB1, CD59, COLEC12, IL1RL1, IL13RA1, CXADR, TNFSF13, IL34, LILRB1	LPO, CCL22, CTSV, IL15, CLEC4A, PRKCQ, IL19, TSLP, CCL11, CCL20
3	R-HSA-449147	Signaling by Interleukins	2.09E-12	47	658	TIMP1, IL4R, ICAM1, CSF1, IL18BP, IL18, LYN, HAVCR2, IL12RB1, SDC1, LBP, FASLG, IL20, LGALS9, TNFRSF1B, IL1R1, IL3RA, IFNG, CD4, IL33, CCL4, VCAM1, IL6R, IL12B, TNFRSF1A, ITGB2, ATF2, IL17RB, IL2RA, MMP3, IL10, ITGB1, IL18R1, IL1RL1, IL2RB, IL13RA1, IL10RB, IL34	CCL22, IL15, CCL11, TSLP, IL19, CCL20
4	R-HSA-1280215	Cytokine Signaling in Immune system	9.11E-12	60	1039	TIMP1, IL4R, ICAM1, CSF1, IL18BP, IL18, LYN, HAVCR2, LTA, LTBR, IL12RB1, SDC1, LBP, FASLG, CD27, TNFRSF4, TNFRSF8, IL20, LGALS9, TNFRSF1B, IL1R1, TNFRSF6B, IL3RA, IFNG, CD4, IL33, CCL4, VCAM1, IL6R, TNFSF13B, IL12B, BST2, TNFRSF1A, ITGB2, ATF2, HLA_DRA, IFNGR2, IL17RB, IL2RA, MMP3, IL10, ITGB1, IL18R1, TNFRSF11B, EDA2R, IL1RL1, IL2RB, IL13RA1, IL10RB, TNFSF13, IL34	CCL22, IL15, CCL11, TSLP, IL19, CCL20
5	R-HSA-5669034	TNFs bind their physiological receptors	1.26E-10	11	30	TNFSF13, LTA, TNFSF13B, TNFRSF1B, TNFRSF6B, TNFRSF11B, EDA2R, TNFRSF1A, CD27, TNFRSF4, TNFRSF8	
6	R-HSA-1280218	Adaptive Immune System	3.25E-10	53	933	SIGLEC9, LILRB2, LILRA2, SLAMF6, ICAM1, LYN, NCR1, CD300LF, ZBTB16, SH2D1A, OSCAR, LILRB4, SIGLEC10, CD79B, BTN2A1, SIGLEC7, CD160, LAIR2, LAIR1, CD99, NFATC3, CD74, PPP3R1, PDCD1LG2, CD4, KLRB1, ICAM2, CD200R1, VCAM1, ICAM3, CTSL, PILRA, ITGB2, PDCD1, BTN3A2, CD14, CD300C, HLA_DRA, NECTIN2, LILRB5, KIR2DL3, CRTAM, SIGLEC6, CD300E, SLAMF7, ITGB1, SIGLEC1, COLEC12, KLRD1, CXADR, LILRB1	CTSV, PRKCQ
7	R-HSA-216083	Integrin cell surface interactions	1.51E-09	15	86	ITGB1, ITGA5, VWF, ICAM3, ICAM1, COL6A3, COL4A1, HSPG2, ICAM2, VCAM1, COL18A1, ITGB2, TNC, COL9A1	ITGA11
8	R-HSA-1474244	Extracellular matrix organization	7.95E-09	27	328	TIMP1, ITGB1, VWF, ICAM3, ICAM1, NID2, MMP3, NID1, SDC1, VCAN, COL18A1, ADAM8, HSPG2, TNC, VCAM1, CTSL, ITGA5, ADAM15, CEACAM1, EFEMP1, COL6A3, COL4A1, ICAM2, ITGB2, COL9A1	ITGA11, CTSV
9	R-HSA-6783783	Interleukin-10 signaling	9.65E-08	13	86	TIMP1, ICAM1, CSF1, IL10RB, IL18, IL12B, TNFRSF1B, IL1R1, TNFRSF1A, CCL4, IL10	CCL20, CCL22
10	R-HSA-381426	Regulation of Insulin-like Growth Factor (IGF) transport and uptake by Insulin-like Growth Factor Binding Proteins (IGFBPs)	2.34E-07	15	127	TIMP1, CST3, CCN1, SPARCL1, IGFBP6, CSF1, FSTL3, PROC, IGFBP4, GZMH, GAS6, IGFBP7, VCAN, TNC, VWA1	
11	R-HSA-8957275	Post-translational protein phosphorylation	0.00000134	13	109	TIMP1, CST3, CCN1, SPARCL1, CSF1, FSTL3, PROC, IGFBP4, GAS6, IGFBP7, VCAN, TNC, VWA1	
12	R-HSA-202733	Cell surface interactions at the vascular wall	0.00000168	20	257	ITGB1, ITGA5, THBD, CD48, CXADR, TNFRSF10B, PROC, LYN, CD99, CEACAM1, GAS6, CD244, PSG1, CD74, TEK, SELE, SDC1, ITGB2, ANGPT2	L1CAM
13	R-HSA-5668541	TNFR2 non-canonical NF-kB pathway	0.00000475	12	104	TNFSF13, LTA, TNFSF13B, TNFRSF1B, TNFRSF6B, TNFRSF11B, EDA2R, LTBR, TNFRSF1A, CD27, TNFRSF4, TNFRSF8	
14	R-HSA-380108	Chemokine receptors bind chemokines	0.00000649	9	57	CXCL9, CCL4, XCL1, CXCL11	CCL20, CCL11, CX3CL1, CCL22, CXCL16
15	R-HSA-6785807	Interleukin-4 and Interleukin-13 signaling	0.0000065	17	211	TIMP1, ITGB1, FASLG, IL6R, IL4R, ICAM1, IL13RA1, IL18, IL12B, TNFRSF1B, MMP3, LBP, VCAM1, ITGB2, IL10	CCL11, CCL22

Supplementary Table 5 | Table of statistically significant REZPEG-modulated proteins grouped by pathway. Pathway analysis of dose-dependent and statistically significant differences in protein expression in response to REZPEG treatment compared to placebo using the Reactome knowledgebase. Source data are provided as a Source Data file.

Supplementary Table 6 | Sample numbers for psoriasis pharmacokinetic and pharmacodynamic analyses

Supplementary Table 6 | Sample numbers for psoriasis pharmacokinetic and pharmacodynamic analyses

	Wk0	Wk1-D5	Wk1-D8	Wk1.5	Wk2	Wk3	Wk4	Wk6	Wk8	Wk10	Wk12
Pharmacokinetics (ng/mL)											
24 µg/kg, n	20	21	15	20	18	18	15	13	11	10	11
$CD25^{bright}$ Tregs (cells/µl)											
Placebo, n	4	2	3		2	4	4		2		3
24 µg/kg, n	20	19	16		14	15	12		9		7
$CD25^{bright}$ Tregs (fold change from baseline, cells/µl)											
Placebo, n	4	2	3		2	4	4		2		3
24 µg/kg, n	19	18	15		13	14	11		8		7
$CD25^{bright}$ Tregs (%CD4+ T cells)											
Placebo, n	4	2	3		2	4	4		2		3
24 µg/kg, n	20	19	16		14	14	11		9		7
Total Tregs (cells/µl)											
Placebo, n	4	2	3		2	4	4		2		3
24 µg/kg, n	20	18	17		14	15	12		10		7
Total Tregs (%CD4+ T cells)											
Placebo, n	4	2	3		2	4	4		2		4
24 µg/kg, n	20	19	16		14	13	11		9		7
CD4+ T cells (cells/µl)											
Placebo, n	4	2	3		2	4	4		2		3
24 µg/kg, n	20	19	16		14	15	12		9		7
CD4+ T cells (fold change from baseline, cells/µl)											
Placebo, n	4	2	3		2	4	4		2		3
24 µg/kg, n	20	18	16		14	15	12		9		7
CD8+ T cells (cells/µl)											
Placebo, n	4	2	3		2	4	4		2		3
24 µg/kg, n	20	19	16		14	15	12		11		7
CD8+ T cells (fold change from baseline, cells/µl)											
Placebo, n	4	2	3		2	4	4		2		3
24 µg/kg, n	20	18	16		14	15	12		11		7
CD3-CD56+ NK (cells/µl)											
Placebo, n	5	2	3		2	3	4		3		4
24 µg/kg, n	21	18	15		15	16	14		13		10
$CD3\text{-}CD56^{bright}$ (%CD56+ NK cells)											
Placebo, n	4	2	3		2	4	4		2		4
24 µg/kg, n	20	19	16		14	13	11		9		7
$CD3\text{-}CD56^{dim}$ (%CD56+ NK cells)											
Placebo, n	4	2	3		2	4	4		2		4
24 µg/kg, n	20	19	16		14	13	11		9		7

Supplementary Table 7 | Sample numbers for atopic dermatitis pharmacokinetic and pharmacodynamic analyses

Supplementary Table 7 | Sample numbers for atopic dermatitis pharmacokinetic and pharmacodynamic analyses

	Wk0	Wk1-D5	Wk1-D8	Wk1.5	Wk2	Wk3	Wk4	Wk6	Wk8	Wk10	Wk12
Pharmacokinetics (ng/mL)											
12 µg/kg, n	14	13	13	14	14	14	10	15	13	12	11
24 µg/kg, n	15	14	14	17	16	16	13	16	14	12	12
$CD25^{bright}$ Tregs (cells/µl)											
Placebo, n	8	8	9		8	5	7		5		4
12 µg/kg, n	14	7	9		12	9	6		9		7
24 µg/kg, n	16	11	8		14	10	10		12		11
$CD25^{bright}$ Tregs (fold change from baseline, cells/µl)											
Placebo, n	8	7	7		7	5	6		5		3
12 µg/kg, n	14	7	8		11	8	6		8		7
24 µg/kg, n	15	10	8		13	9	10		11		9
$CD25^{bright}$ Tregs (%CD4+ T cells)											
Placebo, n	8	8	8		8	7	6		5		5
12 µg/kg, n	14	7	9		12	9	6		8		7
24 µg/kg, n	16	11	8		13	10	10		12		11
Total Tregs (cells/µl)											
Placebo, n	8	8	9		8	6	7		5		4
12 µg/kg, n	14	7	9		12	9	6		8		7
24 µg/kg, n	16	11	8		14	10	10		12		11
Total Tregs (%CD4+ T cells)											
Placebo, n	8	8	8		8	6	7		5		5
12 µg/kg, n	14	7	9		12	9	6		8		7
24 µg/kg, n	16	11	8		13	10	10		12		11
CD4+ T cells (cells/µl)											
Placebo, n	8	8	9		7	5	7		5		5
12 µg/kg, n	14	7	9		12	9	6		8		7
24 µg/kg, n	16	11	8		14	10	10		12		11
CD4+ T cells (fold change from baseline, cells/µl)											
Placebo, n	8	7	7		6	5	6		5		4
12 µg/kg, n	14	7	8		11	8	6		7		7
24 µg/kg, n	15	11	8		12	10	10		11		10
CD8+ T cells (cells/µl)											
Placebo, n	8	8	9		7	5	7		5		5
12 µg/kg, n	14	7	9		12	9	6		8		7
24 µg/kg, n	16	11	8		13	10	10		12		11
CD8+ T cells (fold change from baseline, cells/µl)											
Placebo, n	8	7	7		6	5	6		5		4
12 µg/kg, n	14	7	8		11	8	6		7		7
24 µg/kg, n	15	11	8		11	10	10		11		10
CD3-CD56+ NK (cells/µl)											
Placebo, n	10	8	10		7	7	8		9		6
12 µg/kg, n	15	7	10		12	11	10		11		9
24 µg/kg, n	16	12	11		14	12	13		12		12
CD3-$CD56^{bright}$ (%CD56+ NK cells)											
Placebo, n	8	8	8		7	5	7		5		5
12 µg/kg, n	14	7	9		12	9	6		8		7
24 µg/kg, n	16	11	8		13	10	10		12		11
CD3-$CD56^{dim}$ (%CD56+ NK cells)											
Placebo, n	8	8	8		8	5	7		5		5
12 µg/kg, n	14	7	9		12	9	6		8		7
24 µg/kg, n	16	11	8		13	10	10		12		11

Supplementary Table 8 | Psoriasis patient numbers for continuous endpoints

Supplementary Table 8 | PsO patient numbers at continuous endpoints

	Wk0	Wk2	Wk3	Wk4	Wk6	Wk8	Wk10	Wk12	Wk14	Wk16	Wk19
Placebo, n	5	5	5	5	5	5	4	5	4	5	5
24 µg/kg, n	21	18	17	14	13	12	11	11	11	11	11

Supplementary Table 9 | Atopic dermatitis patient numbers for continuous endpoints

Supplementary Table 9 | AD patient numbers at continuous endpoints

	Wk0	Wk2	Wk3	Wk4	Wk6	Wk8	Wk10	Wk12	Wk14	Wk16	Wk19	Wk24	Wk28	Wk32	Wk36	Wk40	Wk44	Wk48
Placebo, n	10	8	6	8	6	8	5	7	5	5	6	1	2	1	1	1	1	1
12 µg/kg, n	16	16	15	15	14	14	12	12	12	12	12	7	5	5	5	4	3	4
24 µg/kg, n	17	16	16	15	15	14	13	12	13	13	13	8	9	9	7	7	7	7

Supplementary Table 10 | Sample numbers for serum proteomic biomarker analyses

Supplementary Table 10 | Sample numbers for serum protein biomarker analyses

	Wk0	Wk2	Wk3	Wk4	Wk12
Placebo, n	8	8	8	8	8
12 µg/kg, n	16	16	16	15	12
24 µg/kg, n	16	16	16	14	12

Supplementary Table 11 | Rescue medications for the indication of atopic dermatitis

Supplementary Table 11 | Rescue medications for the indication of atopic dermatitis

Number of patients, n (%)	Pooled Placebo N=10	10 µg/kg REZPEG N=1	12 µg/kg REZPEG N=16	24 µg/kg REZPEG N=17	Overall REZPEG N=34
Use of any rescue medication - on treatment	1 (10)	0	0	0	0
Triamcinolone/Triamcinolone acetonide 0.1%	1 (10)	0	0	0	0
Use of any rescue medication - during follow-up	0	0	2 (12.5)	1 (5.9)	3 (8.8)
Triamcinolone/Triamcinolone acetonide 0.1%	0	0	1 (6.3)	1 (5.9)	2 (5.9)
Prednisone	0	0	1 (6.3)	0	1 (2.9)

Supplementary Table 12 | Source antibodies used for pharmacokinetic and pharmacodynamic assessments

Supplementary Table 12 | Source antibodies used for pharmacokinetic and pharmacodynamic assessments

Antibody	Supplier	Cat. No.	Stock Conc.	Final Conc.
Mouse anti-human IL-2	Eli Lilly	Custom	7.18 mg/mL	1 µg/mL
Mouse anti-human IL-2	MabTech	3445-5-1000	0.5 mg/mL	1 µg/mL
Rabbit biotin anti-PEG	Abcam	ab53449	0.01 mg/mL	0.05 µg/mL
BB515 mouse anti-human CD25	BD Biosciences	564467	100 tests	5 µL/test
PE mouse anti-human CD8	BD Biosciences	555367	100 tests	20 µL/test
PerCP-Cy5.5 mouse anti-human CD3	BD Biosciences	340949	3.0 µg/mL	0.06 µg/mL (20 µL/test)
PE-Cy7 mouse anti-human CD56	BD Biosciences	335791	25 µg/mL	0.125 µg/mL (5 µL/test)
AF647 mouse anti-human FoxP3	BD Biosciences	560045	100 tests	20 µL/test
APC-H7 mouse anti-human CD45	BD Biosciences	560178	100 tests	5 µL/test
BV421 mouse anti-human Ki67	BD Biosciences	562899	50 tests	5 µL/test
BV510 mouse anti-human CD4	BD Biosciences	562970	100 tests	5 µL/test

Supplementary References

1. Fanton, C., et al. Selective expansion of regulatory T cells by NKTR-358 in healthy volunteers and patients with systemic lupus erythematosus. *J. Transl. Autoimmun.* **5**, 100152 (2022).