

SUPPLEMENTARY MATERIALS

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Safety and Efficacy of ALRV5XR in Men with Androgenetic Alopecia: A Randomised, Double-Blinded, Placebo-Controlled Clinical Trial

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Table S1. Abbreviations

Text Abbreviations	
AGA	Androgenetic Alopecia
BVM	Botanical, Vitamin and Mineral
FDA	Food and Drug Administration
FPHL	Female Pattern Hair Loss
HF	Hair Follicle
HFSC	Hair Follicle Stem Cell
HL	Hair Loss
MOA	Mechanism of Action
MPHL	Male Pattern Hair Loss
QoL	Quality of Life
SC	Stem Cell
TAHC	Target Area Hair Count
TE	Telogen Effluvium
TH	Terminal Hair
THC	Terminal Hair Count
VH	Vellus Hair
Units of Measure	
CI	Confidence Interval
cm	Centimetre
µm	Micrometre
mm	Millimetre
OR	Odds Ratio
%	Per cent
p	Statistical Probability – T-Test
F	Fisher Statistic - ANOVA Test
Growth Factors	
EGF	Epidermal Growth Factor
FGF-7	Fibroblast Growth Factor – 7
FGF-18	Fibroblast Growth Factor – 18
HGF	Hepatocyte Growth Factor
IGF	Insulin Growth Factor
KGF	Keratinocyte Growth Factor
VEGF	Vascular Endothelial Growth Factor
Dermal Papilla cell and Stem Cell stimulation	
BMP	Bone Morphogenic Proteins
mTORC1	Mammalian Target of Rapamycin – 1
PKC	Protein Kinase C
PPAR γ	Peroxisome Proliferator-Activated Receptor Gamma
Shh	Sonic Hedgehog
Wnt	Wingless-related integration site
Immunomodulation	
COX	Cyclooxygenase
IFN- α	Interferon-alpha
IFN- γ	Interferon-gamma
IL-1b, IL-6 and IL-12	Interleukins -1b, 6, -12
NF- $\kappa\beta$	Nuclear Factor Kappa Beta
PGE2	Prostaglandin E2
PGD2	Prostaglandin D2
TNF- α ,	Tumour Necrosis Factor alpha
TGF- β	Transformation Growth Factor beta
Androgens & Mediators	
5 α -R	5 α -Reductase
DHT	Dihydrotestosterone

Table S2. ALRV5XR Material Active Ingredients

Active Ingredients*	
Oral (capsule)	Angelica sinensis, Ascophyllum nodosum, Astragalus membranaceus, Biotin, Coenzyme Q10, Copper, Eclipta prostrata, Folate, Ganoderma lucidum, Malus domestica, Moringa oleifera, Niacin, Pantothenic acid, Polygonum multiflorum, Punica granatum, Riboflavin, Rosmarinus officinalis, Scutellaria baicalensis, Selenium, Silicon, Sophora flavescens, Vitamin A, Vitamin B6, Vitamin B7(Biotin), Vitamin B12, Vitamin D, Vitis vinifera, and Zinc
Shampoo	Caffeine, Eclipta prostrata, Lupinus, Momordica charantia, Moringa oleifera, Pyrus malus, Rosmarinus officinalis, Vitis vinifera, Scutellaria baicalensis, Vitamin B7(Biotin)
Conditioner	Caffeine, Eclipta prostrata, Lupinus, Momordica charantia, Moringa oleifera, Pyrus malus, Rosmarinus officinalis, Vitis vinifera, Scutellaria baicalensis, Vitamin B7(Biotin)
Follicle serum	Caffeine, Eclipta prostrata, Lupinus, Momordica charantia, Moringa oleifera, Ocimum basilicum, Pisum sativum, Pyrus malus, Rosmarinus officinalis, Vitis vinifera, Scutellaria baicalensis, Vitamin B7(Biotin)

*Patents pending

Table S3: Laboratory and Physical Exam Results. At trial completion, there were statistically significant differences between the groups (highlighted in grey) for serum Albumin, HDL Cholesterol and Platelets. These differences were within the normal range, except for Albumin, which was slightly above the normal range for both groups, however, the ALRV5XR group was trending towards the normal range. These differences were determined not clinically relevant.

Table S3a: Blood Laboratory Results.

			Placebo									ALRV5XR									Placebo vs ALRV5XR					
			Baseline			12 Weeks			24 Weeks			Baseline			12 Weeks			24 Weeks			T-Tests P-Value (Placebo vs. ALRV5XR)					
Analyte	UOM	Reference Range	N	Mean	Stddev	N	Mean	Stddev	N	Mean	Stddev	N	Mean	Stddev	N	Mean	Stddev	N	Mean	Stddev	BL	BL - 12 Weeks	BL - 24 Weeks	12 - 24 Weeks		
Blood:																										
Albumin	g/dL	3.4-4.2	18	4.47	0.213	16	4.54	0.247	17	4.55	0.245	21	4.42	0.291	16	4.40	0.262	16	4.33	0.316	0.535	0.186	0.015	0.045		
Alkaline Phosphatase	IU/L	46-119	18	69.44	13.929	16	68.31	13.190	17	68.24	12.996	21	71.05	19.800	16	69.81	19.793	16	74.38	17.663	0.781	0.384	0.771	0.176		
ALT (SGPT)	IU/L	0-29	18	25.06	18.969	16	25.31	13.967	17	23.24	12.120	21	36.81	40.014	16	34.69	31.492	16	31.75	18.663	0.274	0.406	0.796	0.737		
AST (SGOT)	IU/L	0-120	18	24.89	9.533	16	24.56	8.888	17	22.94	7.787	21	24.57	6.884	16	29.69	19.924	16	23.75	7.980	0.907	0.291	0.945	0.516		
Baso (Absolute)	x10E3/uL	0.0-0.6	18	0.02	0.037	16	0.03	0.043	17	0.02	0.038	21	0.01	0.035	16	0.02	0.039	16	0.03	0.046	0.842	0.564	0.441	0.186		
Basos	%	Not Estab.	18	0.67	0.577	16	0.50	0.500	17	0.47	0.499	21	0.57	0.495	16	0.69	0.583	16	0.63	0.484	0.592	0.103	0.173	0.410		
Bilirubin, Total	mg/dL	0.0-1.2	18	0.54	0.254	16	0.50	0.250	17	0.59	0.253	21	0.57	0.334	16	0.49	0.287	16	0.49	0.245	0.786	0.584	0.146	0.262		
BUN	mg/dL	6-24	18	14.83	2.774	16	15.63	2.997	17	15.71	3.706	21	15.33	4.663	16	16.50	2.449	16	15.00	3.354	0.700	0.952	0.502	0.174		
Calcium	mg/dL	8.6-10.4	18	9.40	0.269	16	9.45	0.341	17	9.33	0.349	21	9.48	0.384	16	9.48	0.283	16	9.39	0.325	0.496	0.294	0.654	0.723		
Carbon Dioxide, Total	mmol/L	16-29	18	24.89	1.882	16	24.56	2.474	17	24.06	2.100	21	25.62	1.588	16	24.69	2.256	16	22.88	1.166	0.209	0.969	0.109	0.432		
Chloride	mmol/L	96-106	18	100.39	1.976	16	101.19	2.242	17	101.35	1.780	21	100.81	2.788	16	102.19	1.590	16	102.44	1.456	0.605	0.084	0.104	0.756		
Cholesterol, Total	mg/dL	100-169	18	174.78	38.888	16	188.69	28.504	17	174.47	30.817	21	203.19	34.436	16	207.38	40.009	16	185.56	36.975	0.024	0.151	0.274	0.936		
C-Reactive Protein, Cardiac	mg/L	0.00-3.00	17	1.78	3.038	16	1.59	2.468	17	1.70	2.044	21	1.99	2.031	16	2.46	3.632	16	2.24	2.666	0.807	0.769	0.408	0.649		
Creatinine	mg/dL	0.4-1.19	18	0.93	0.114	16	0.99	0.107	17	0.96	0.148	21	0.94	0.170	16	0.98	0.167	16	0.91	0.143	0.791	0.688	0.888	0.902		
eGFR If Africn Am	mL/min/1.73	>59	18	111.83	13.777	16	104.75	12.467	16	109.63	17.084	21	108.48	17.565	16	105.75	19.337	16	111.25	17.181	0.527	0.480	0.778	0.805		
eGFR If Nofricn Am	mL/min/1.73	>59	18	96.78	11.914	16	90.50	10.671	16	94.69	14.696	21	94.00	15.191	16	91.44	16.677	16	96.38	14.887	0.545	0.480	0.730	0.832		
Eos	%	Not Estab.	18	2.72	1.520	16	2.63	2.088	17	2.12	1.409	21	2.90	1.269	16	3.25	1.199	16	2.88	1.364	0.693	0.646	0.217	0.602		
Eos (Absolute)	x10E3/uL	0.0-0.6	18	0.16	0.117	16	0.19	0.175	17	0.12	0.094	21	0.19	0.106	16	0.23	0.083	16	0.21	0.103	0.347	0.600	0.380	0.284		
Glucose	mg/dL	65-99	18	94.50	8.946	16	93.56	28.346	17	94.29	16.619	21	93.95	8.952	16	96.06	16.690	16	103.00	14.405	0.854	0.346	0.120	0.642		
HDL Cholesterol	mg/dL	>39	18	49.00	7.930	16	48.69	9.231	17	49.29	6.875	21	51.00	8.690	16	48.75	12.070	16	45.25	6.505	0.472	0.517	0.044	0.166		
Hematocrit	%	31.9-57.2	18	43.34	2.959	16	43.70	3.671	17	42.41	3.435	21	44.22	2.867	16	44.35	2.295	16	43.99	2.369	0.362	0.420	0.426	0.301		
Hemoglobin	g/dL	10.7-20.5	18	14.51	1.068	16	14.54	1.243	17	14.21	1.301	21	14.75	1.213	16	14.71	1.036	16	14.59	1.067	0.536	0.638	0.378	0.355		
Immature Grans (Abs)	x10E3/uL	Not Estab.	18	0.00	0.000	15	0.00	0.000	17	0.00	0.000	21	0.00	0.021	16	0.01	0.024	16	0.01	0.024	0.361	1.000	1.000	1.000		
Immature Granulocytes	%	Not Estab.	18	0.06	0.229	15	0.00	0.000	17	0.06	0.235	21	0.19	0.499	16	0.19	0.390	16	0.13	0.331	0.311	0.948	0.677	0.170		
INR	N	0.8-1.2	18	1.03	0.047	16	1.03	0.043	17	1.05	0.061	21	1.02	0.039	15	1.01	0.034	16	1.04	0.048	0.321	0.326	0.477	0.106		
Insulin	uIU/mL	2.6-24.9	19	10.07	6.510	16	21.41	24.915	16	16.90	16.183	19	12.78	9.982	16	30.81	31.045	16	32.73	35.052	0.342	0.648	0.336	0.624		
LDL Cholesterol Calc	mg/dL	0-109	18	104.11	35.559	16	109.25	28.904	16	98.06	24.608	21	126.62	31.347	15	123.73	36.547	15	101.20	22.956	0.048	0.295	0.452	0.849		
Lymphs	%	Not Estab.	18	33.28	6.296	16	30.81	7.764	17	30.12	7.925	21	34.00	7.764	16	33.75	8.151	16	32.75	10.103	0.760	0.175	0.260	0.761		
Lymphs (Absolute)	x10E3/uL	0.9-5.0	18	1.82	0.484	16	2.02	0.526	17	1.71	0.484	21	2.20	0.627	16	2.23	0.618	16	2.15	0.654	0.047	0.123	0.572	0.303		
Magnesium	mg/dL	1.6-2.4	18	2.14	0.111	16	2.08	0.151	17	2.07	0.102	21	2.17	0.145	16	2.13	0.148	16	2.10	0.132	0.455	0.852	0.879	0.421		
MCH	pg	26.1-38.7	18	29.28	2.523	16	29.32	2.731	17	29.26	2.605	21	29.81	2.332	16	29.73	2.380	16	29.63	2.512	0.506	0.725	0.149	0.168		
MCHC	g/dL	31.9-36.8	18	33.48	1.052	16	33.28	1.063	17	33.48	0.741	21	33.32	0.883	16	33.16	1.055	16	33.15	1.074	0.619	0.687	0.795	0.706		
MCV	fL	79-110	18	87.33	6.791	16	87.94	6.995	17	87.35	6.721	21	89.43	5.786	16	89.63	6.071	16	89.31	6.400	0.317	0.950	0.292	0.123		
Monocytes	%	Not Estab.	18	7.67	2.082	16	7.81	1.424	17	7.76	2.263	21	8.00	1.799	16	7.44	1.731	16	7.50	1.458	0.604	0.604	0.142	0.391	0.690	
Monocytes(Absolute)	x10E3/uL	0.2-1.3	18	0.41	0.110	16	0.51	0.122	17	0.43	0.118	21	0.54	0.191	16	0.49	0.130	16	0.50	0.137	0.021	0.001	0.062	0.061		
Neutrophils	%	Not Estab.	18	55.61	7.447	16	57.81	7.410	17	59.47	9.300	21	54.33	8.374	16	54.69	9.432	16	56.13	10.816	0.629	0.329	0.285	0.903		
Neutrophils (Absolute)	x10E3/uL	1.2-6.1	18	3.12	0.991	16	3.88	1.101	17	3.45	1.026	21	3.62	1.124	16	3.67	0.887	16	3.77	1.012	0.161	0.011	0.063	0.151		
Phosphorus	mg/dL	2.5-7.1	18	3.27	0.421	16	3.50	0.582	17	3.16	0.511	21	3.20	0.453	16	3.29	0.597	16	2.94	0.579	0.644	0.424	0.311	0.808		
Platelets	x10E3/uL	140-396	18	270.44	59.770	16	272.13	56.253	17	247.88	43.710	21	267.52	43.177	16	251.25	40.172	16	277.75	44.463	0.864	0.139	0.102	0.013		
Potassium	mmol/L	3.7-5.2	18	4.51	0.205	16	4.47	0.293	17	4.50	0.243	21	4.42	0.374	16	4.38	0.248	16	4.34	0.333	0.370	0.938	0.621	0.577		
Prothrombin Time	sec	10.2-15.4	18	10.48	0.289	16	10.44	0.341	17	10.60	0.485	21	10.27	0.360	15	10.19	0.360	16	10.38	0.419	0.059	0.512	0.521	0.176		
RBC	x10E6/uL	3.68-5.77	18	4.98	0.413	16	4.99	0.432	17	4.87	0.374	21	4.97	0.447	16	4.96	0.253	16	4.95	0.406	0.937	0.407	0.807	0.569		
RDW	%	12.1-16.9	18	13.89	1.142	16	14.24	1.163	17	13.98	0.859	21	13.90	0.961	16	13.75	0.839	16	13.77	0.820	0.975	0.002	0.418	0.283		
Sodium	mmol/L	134-144	18	140.72	1.557	16	140.81	2.038	17	140.76	2.237	21	141.52	2.038	16	140.50	1.768	16	141.06	0.827	0.193	0.315	0.859	0.529		
Triglycerides	mg/dL	0-74	18	108.50	57.696	16	153.38	65.116	17	148.94	97.428	21	128.00	60.768	16	180.69	97.521	16	188.63	122.040	0.326	0.907	0.958	0.852		
TSH	uIU/mL	0.700																								

Table S3b: Urine Laboratory Results.

			Placebo									ALRV5XR									Placebo vs ALRV5XR					
			Baseline			12 Weeks			24 Weeks			Baseline			12 Weeks			24 Weeks			T-Tests P-Value (Placebo vs. ALRV5XR)					
Analyte	UOM	Reference Range	N	Mean	Stddev	N	Mean	Stddev	N	Mean	Stddev	N	Mean	Stddev	N	Mean	Stddev	N	Mean	Stddev	BL	BL - 12 Weeks	BL - 24 Weeks	12 - 24 Weeks		
Urine:																										
Alb/Creat Ratio	mg/g creat	0.0-30.0	18	4.74	4.535	16	4.36	3.242	17	3.86	2.480	21	12.90	29.818	16	5.96	7.800	16	14.06	24.084	0.270	0.495	0.722	0.191		
Albumin, Urine	ug/mL	Not Estab.	18	7.97	8.961	16	5.76	4.177	17	5.58	4.439	21	18.10	44.045	16	8.40	11.427	16	24.47	42.448	0.356	0.732	0.779	0.198		
Creatinine, Urine	mg/dL	Not Estab.	18	174.93	82.364	16	151.26	75.552	17	158.31	80.166	21	138.19	67.787	16	141.09	72.827	16	157.72	62.722	0.145	0.610	0.326	0.954		
pH		5.0-7.5	18	5.86	0.847	16	5.69	0.527	17	6.26	0.987	21	5.98	0.932	16	5.84	0.896	16	6.19	0.827	0.698	0.949	0.314	0.646		
Specific Gravity		1.005-1.030	18	1.02	0.007	16	1.02	0.007	17	1.02	0.008	21	1.02	0.007	16	1.02	0.007	16	1.02	0.006	0.236	0.970	0.417	0.956		
Urobilinogen, Semi-Qn	mg/dL	0.2-1.0	18	0.29	0.251	16	0.25	0.194	17	0.34	0.305	21	0.24	0.170	16	0.25	0.194	16	0.30	0.265	0.471	0.964	0.521	0.680		

Table S3c: Physical Exam Results.

			Placebo									ALRV5XR									Placebo vs ALRV5XR					
			Baseline			12 Weeks			24 Weeks			Baseline			12 Weeks			24 Weeks			T-Tests P-Value (Placebo vs. ALRV5XR)					
Analyte	UOM	Reference Range	N	Mean	Stddev	N	Mean	Stddev	N	Mean	Stddev	N	Mean	Stddev	N	Mean	Stddev	N	Mean	Stddev	BL	BL - 12 Weeks	BL - 24 Weeks	12 - 24 Weeks		
Physical Exam:																										
Height (cm)	cm		22	175.94	12.783	22	175.94	12.783	22	175.95	12.733	22	173.70	9.522	22	173.59	10.298	22	173.93	9.183	0.523	0.927	0.628	0.784		
Weight (kg)	kg		22	84.47	23.029	21	84.17	22.782	19	85.38	22.886	22	84.77	17.277	20	87.13	15.915	18	88.68	13.889	0.962	0.711	0.858	0.903		
BMI	kg/m^2		22	27.25	6.109	21	27.35	5.939	19	27.44	5.515	22	28.26	6.153	20	29.05	5.459	18	29.52	5.534	0.596	0.766	0.791	0.863		
Temperature	deg F		22	96.94	1.600	21	97.72	0.751	19	97.79	0.634	22	97.17	0.679	20	97.81	0.795	18	97.76	0.569	0.552	0.744	0.602	0.575		
RespiratoryRate	bpm		22	15.32	1.519	21	15.43	1.620	19	16.37	2.454	22	16.05	2.602	20	15.75	2.256	17	16.06	1.392	0.275	0.092	0.364	0.743		
BP-L DIA	mmHg		22	85.91	11.623	20	82.30	11.424	18	81.17	10.194	22	84.95	18.428	20	88.55	15.781	18	85.56	19.511	0.842	0.350	0.477	0.388		
BP-L SYS	mmHg		22	128.41	12.405	21	127.00	15.850	19	125.11	15.960	22	128.82	21.670	20	133.60	17.656	18	131.94	20.101	0.941	0.579	0.753	0.650		
BP-R DIA	mmHg		20	82.20	10.328	21	83.81	9.205	19	79.68	10.563	22	83.77	18.218	20	86.85	12.167	18	83.56	17.765	0.742	0.994	0.817	0.826		
BP-R SYS	mmHg		20	129.00	15.821	21	124.48	14.381	19	127.37	15.401	22	127.32	21.007	20	128.70	18.725	18	129.28	18.535	0.778	0.800	0.945	0.497		
Mean BP DIA	mmHg		22	84.11	9.628	21	83.07	9.963	19	81.42	9.967	22	84.36	17.561	20	87.70	12.743	18	84.56	15.404	0.955	0.640	0.765	0.453		
Mean BP SYS	mmHg		22	128.34	13.229	21	125.98	13.616	19	126.26	15.076	22	128.07	21.015	20	131.15	15.750	18	130.61	13.141	0.960	0.653	0.859	0.502		
Heart rate	bpm		22	77.27	11.258	21	78.29	12.279	19	82.58	12.504	22	77.05	14.537	20	75.10	10.094	17	77.76	9.478	0.955	0.335	0.106	0.496		

Table S4: Adverse Events. No adverse events (AE's) or serious adverse events (SAE's) were reported in either the ALRV5XR or Placebo groups. A list of AE's typically reported in clinical trials of AGA are identified.

Possible Adverse Events
Acne
Burning/Stinging
Decreased Libido
Desquamation/Dandruff
Elevated Blood Pressure
Erythema
Feeling of Skin Tension
Folliculitis
Gastrointestinal Complaints/Stomach Upset
Headache
Joint Stiffness
Malaise and Fatigue
Mood Disorders
Neurology-related Complaints
Papules
Peripheral Edema/Fluid Retention
Pruritus
Sexual Dysfunction
Skin Disorders

Table S5: ALRV5XR Responder Distribution. For the ALRV5XR treatment group, the **Change in Terminal Hairs/cm²** shows a significant shift of subjects' hair count changes with a relatively even distribution of 0-20 TH/cm² at week 12. Non-responders from week 12 began to respond by week 24 increasing the proportion of low responders. The overall changes at week 24 show an increased terminal regrowth rate separating into a trimodal effect of low responders increasing density between 0 and 5 THs/cm² (45·5%), moderate responders increasing density 10-20 THs/cm² (36·4%), and high responders regrowing more than 25 THs/cm² (18·2%). The **Per Cent Change in Terminal Hairs** also shows a significant shift of subjects' hair % changes at week 12, increasing regrowth at week 24 to more uniform distribution for moderate and high responders and increasing the proportion of low responders from the population of non-responders at 12 weeks.

	Week 0-12	Week 0-24
Change in Terminal Hairs/cm²		
0-5	30·0%	45·5%
5-10	30·0%	-
10-15	20·0%	27·3%
15-20	10·0%	9·1%
20-25	-	-
≥25	10·0%	18·2%
Per Cent Change in Terminal Hairs		
0-5%	50·0%	45·5%
5-10%	30·0%	9·1%
10-15%	-	18·2%
15-20%	-	9·1%
20-25%	20·0%	9·1%
≥25%	-	9·1%

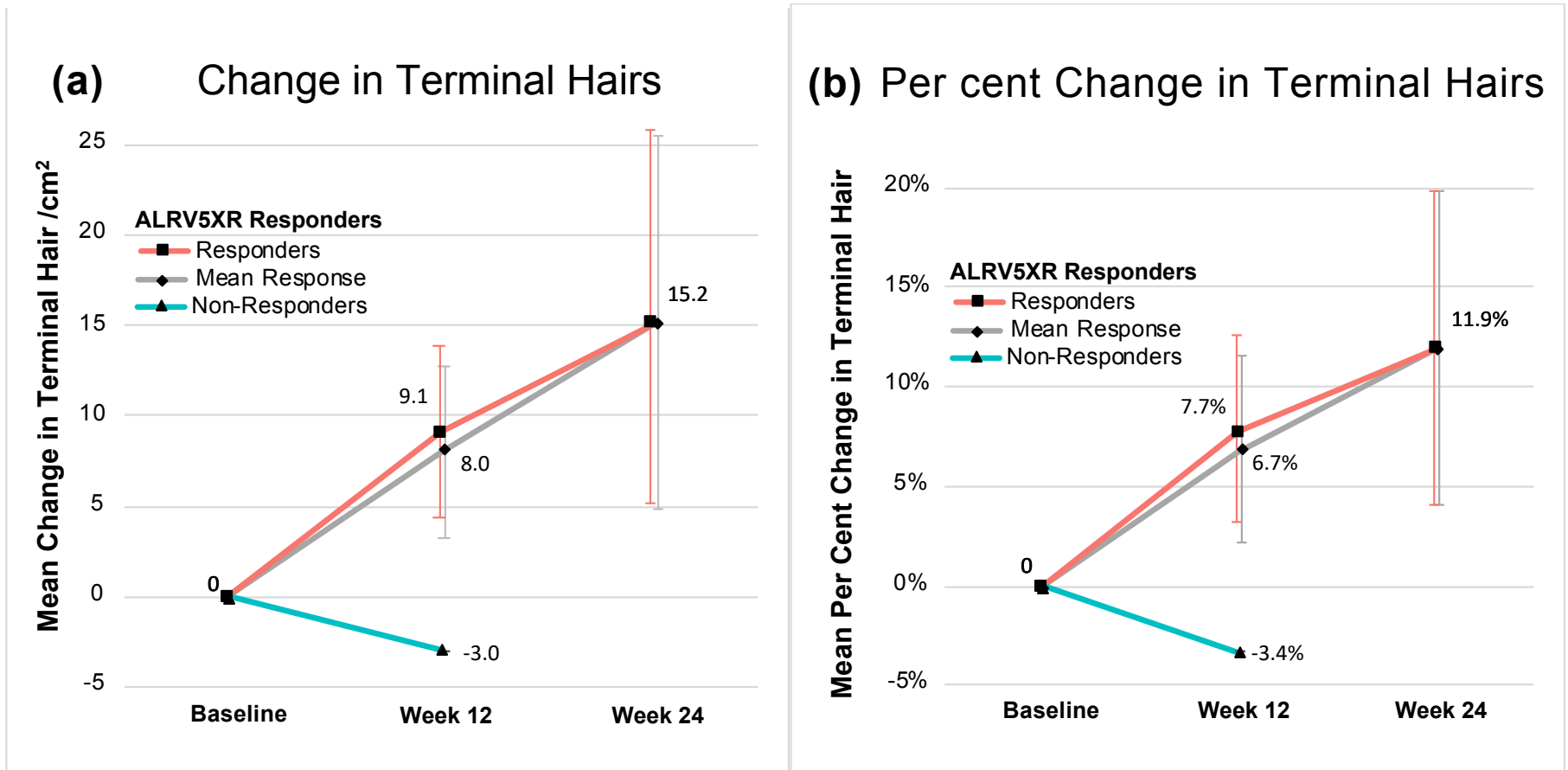


Figure S1. ALRV5XR treatment group changes in Terminal Hair. (a) Changes per cm². (b) Changes by per cent. The mean regrowth response rate within the ALRV5XR group showed a statistically significant increase from baseline ($P_{12\text{weeks}} = 0.0099$ and $P_{24\text{weeks}} < 0.0190$). Non-responders in the first 12 weeks began to regrow hair in the 12 - 24 week period and by week 24, all initial non-responders had become responders. 95% Confidence Intervals for each response group are shown.

Appendix S1: Supplementary Statistical Methods

Mean changes from baseline were analysed using a restricted maximum likelihood based repeated measures approach in combination with the Newton Raphson Algorithm. Analyses include the fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as the continuous, fixed covariates of baseline score and baseline score-by-visit interaction. A-common unstructured covariance structure was used to model the within-patient errors. When this analysis failed to converge, structures were tested in a subsequent order until model-convergence was achieved. The Kenward-Roger approximation was used to estimate denominator degrees of freedom. Significance tests were based on least-squares means using a two-sided $\alpha = 0.05$ (two-sided 95% confidence intervals). The primary treatment comparisons, were the contrast between treatments at the endpoint visit. (*Hackl S, et al, 2019*)