

**Supplemental Information**

**Gene Therapy Intervention in Neovascular  
Eye Disease: A Recent Update**

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Status of Studies found including "Recruiting", "Not yet recruiting", "Active", "not recruiting", "Completed", "Enrolling by invitation", and "Unknown status Studies".

Agents that specifically neutralising VEGF, as well as suppressing PDGF and Angiopoietins/Tie-2 were excluded.

Agents that are classified as steroid, vitamin analogue, NSAID, anti-oxidant, herbal extract; daily supplementary, cell-based therapy, photodynamic therapy, or uncertain mechanism were excluded.

Conditions	Identifier	Drug	Class	Route	Type	Abbreviation:
nAMD	NCT02022501 NCT02401945	DE-120	Receptor tyrosine kinase inhibitor for VEGFR/PDGFR	IVT	small molecule	CCR = CC chemokine receptor CSF1R = Colony stimulating factor 1 receptor DME = diabetic macular edema DR = diabetic retinopathy FGF2 = fibroblast growth factor FLT3 = fms-like tyrosine kinase 3 IGF-I = insulin-like growth factor IGF-1R = insulin-like growth factor-1 receptor IGFBP-3 = insulin like growth factor binding protein 3 IRS-1 = insulin receptor substrate 1 IVT = intravitreal injection nAMD = neovascular age-related macular degeneration PDGFR = platelet-derived growth factor receptor PEDF = pigment epithelium-derived factor PIGF = placental growth factor PKC = protein kinase C PPAR $\alpha$ = peroxisome proliferator-activated receptor alpha ROBO4 = roundabout Guidance Receptor 4 ROP = retinopathy of prematurity RVO = retinal vessel occlusion VEGFR = vascular endothelial growth factor receptor
nAMD	NCT00992563	Linifanib; ABT-869; AL-39324	Receptor tyrosine kinase inhibitor for VEGFR/FLT3/PDGFR	eye drop	small molecule	
nAMD	NCT0138632	Vatalanib; PTK787	Receptor tyrosine kinase inhibitor for VEGFR	oral	small molecule	
nAMD; DR	NCT03479372 NCT02022540 NCT02475109	PAN-90806	Receptor tyrosine kinase inhibitor for VEGFR	eye drop	small molecule	
nAMD	NCT03630315	OTX-TKI	Sustained-release receptor tyrosine kinase inhibitor implants for VEGFR	IVT	small molecule	
nAMD	NCT00612456 NCT01134055 NCT01154062 NCT00733304 NCT00463320 NCT01051700	Pazopanib	Multi-targeted receptor tyrosine kinase inhibitor including VEGFR	eye drop/oral	small molecule	
nAMD; DR	NCT00414999	TG-100801	Kinase inhibitor for VEGFR/Src	eye drop	small molecule	
nAMD; DME; RVO	NCT03953079 NCT03249740 NCT04085341	Sunitinib; GB-102	Pan receptor tyrosine kinase inhibitor	IVT	small molecule	
nAMD	NCT01674569 NCT03710863	CM-082; X-82	Receptor tyrosine kinase inhibitor for VEGFR/PDGFR/CSF1R	oral	small molecule	
nAMD; DME	NCT03835884	AR-13503	Kinase inhibitor for Rho/PKC	IVT	small molecule	
nAMD	NCT02076919 NCT02355028	Acrizanib; LHA510	VEGFR2 inhibitor	eye drop	small molecule	
DME	NCT01565148 NCT00886808	iCo-007; ISIS-13650	c-Raf kinase inhibitor	IVT	antisense oligonucleotide	
DME	NCT03635812	Imatinib; YD312	Tyrosine kinases inhibitor not involving VEGFR	oral	small molecule	
nAMD	NCT02914639 NCT02914613	SF0166	$\alpha$ v $\beta$ 3 integrin inhibitor	eye drop	small molecule	
nAMD; DME; DR	NCT01749891 NCT01482871 NCT02348918 NCT02435862	Risuteganiab; Luminate; ALG-1001	Integrin inhibitor	IVT	peptide	
nAMD	NCT00536016	JSM6427	a5 $\beta$ 1 integrin inhibitor	IVT	small molecule	
nAMD	NCT00762093	Volociximab	a5 $\beta$ 1 integrin inhibitor	IVT	antibody	
DME	NCT02914613	SF0166	$\alpha$ v $\beta$ 3 integrin inhibitor	eye drop	small molecule	
DME; DR	NCT03666923	THR-687	Pan integrin inhibitor	IVT	small molecule	
nAMD	NCT03814291	IBI302	VEGF/C3b/C4b inhibitor	IVT	antibody	
nAMD	NCT01830515	CLG561	C3 inhibitor	IVT	antibody	
nAMD	NCT01527500 NCT01255462 NCT01624636 NCT01535950	Tesidolumab; LGF316	C5 inhibitor	IVT	antibody	
nAMD	NCT03362190 NCT00950638 NCT00709527	Zimura; ARC1905	C5 inhibitor	IVT	aptamer	
nAMD	NCT01157065 NCT00473928	POT-4; AL78898A	C3 inhibitor	IVT	peptide	
nAMD	NCT03465709 NCT02461771	pegcetacoplan; APL-2	C3 inhibitor	IVT	peptide	
nAMD	NCT02555306 NCT03211234	Carotuximab; DE-122	Endoglin inhibitor	IVT	antibody	
nAMD	NCT03869684	MT-0814	CCR3 antagonist	intracocular injection	small molecule	
nAMD	NCT03558061 NCT03558074	ALK4290	CCR3 antagonist	oral	small molecule	
nAMD	NCT03633084 NCT04200248	RBM-007	FGF2 inhibitor	IVT	aptamer	
nAMD	NCT01033721 NCT01271270	Palomid 529	mTOR inhibitor	subconjunctival injection	small molecule	
nAMD	NCT02732899 NCT02357342 NCT00304954	Rapamycin; Sirolimus	mTOR inhibitor	IVT/oral	small molecule	
DR	NCT00401115	Rapamycin; MS-R001	mTOR inhibitor	subconjunctival injection	small molecule	
DME	NCT00711490 NCT00656643 NCT00401115	Rapamycin; Sirolimus	mTOR inhibitor	subconjunctival injection/intraocular injection	small molecule	
nAMD	NCT03216538	AS101	IL-1 $\beta$ converting enzyme inhibitor	oral	small molecule	
nAMD	NCT00503022	ACZ885	IL-1 $\beta$ inhibitor	intravenous infusion	antibody	
nAMD	NCT02358899 NCT01485586	hl-con1	Tissue factor inhibitor	IVT	antibody-like protein	
nAMD	NCT03452527	ICON-1	Tissue factor inhibitor	IVT	antibody-like protein	
nAMD	NCT00767949 NCT01414153	Sonepcizumab; IS ONEP; LT1009	Sphingosine 1-phosphate (S1P) inhibitor	IVT	antibody	
nAMD; DR	NCT00346866 NCT00051129 NCT0299507 NCT00058994 NCT00349739 NCT00211458 NCT00041483 NCT00569569 NCT00346957 NCT00211484 NCT00211419 NCT00211406	Anecortave acetate	Angiogenesis inhibitor	posterior juxtacleral depot/sub-tenon injection/sclera injection	small molecule	
nAMD; DR	NCT02727881 NCT02511613 NCT01678963 NCT00094120 NCT00333476 NCT00139282 NCT00089830 NCT01769183	Squalamine Lactate; MSI-1256F	Sodium-hydrogen exchanger NHE3 inhibitor	eye drop	small molecule	
nAMD; DME	NCT00607750 NCT00536692	mecamylamine; ATG003	Endothelial cells-nicotinic acetylcholine receptors inhibitor	eye drop	small molecule	
nAMD	NCT00446654	CGC-11047	Anti-proliferative properties	subconjunctival injections	small molecule	
nAMD; DME	NCT02530918	DS-7080a	ROBO4 inhibitor	IVT	antibody	
nAMD	NCT01570790	Combretastatin A-4 phosphate	Tubulin depolymerization	intravenous infusion	small molecule	
DR	NCT01869933	OC-10X	Tubulin inhibitor	eye drop	small molecule	
nAMD, DME, RVO	NCT02867735 NCT03927690	LKA651	Erythropoietin inhibitor	IVT	small molecule	

nAMD; DR	NCT03022318 NCT03023059 NCT02706977	Carbidopa-levodopa	PEDF stimulator	oral	small molecule
nAMD	NCT00304954	Dacizumab	CD25 inhibitor	intravenous injection	antibody
nAMD; DME	NCT00304954 NCT00695682 NCT00959725	Infliximab	TNF- $\alpha$ inhibitor	intravenous injection/IVT	antibody
DR	NCT00855608	Adalimumab	TNF- $\alpha$ inhibitor	IVT	antibody
DME	NCT03466099 NCT02193113	KVD001	Plasma kallikrein inhibitor	IVT	small molecule
DME; DR	NCT03511898	THR-149	Plasma kallikrein inhibitor	IVT	small molecule
DME	NCT02732951	Bi-1026706	Bradykinin B1 receptor antagonist	oral	NA
DME	NCT01319487	FOV2304	Bradykinin B1 receptor antagonist	eye drop	small molecule
DME; DR	NCT00133952 NCT00090519 NCT00604383 NCT00266695	Ruboxistaurin; LY 333531	PKC $\beta$ inhibitor	oral	small molecule
DME; DR	NCT04187443	MS-553	PKC $\delta$ inhibitor	oral	small molecule
DME; DR	NCT03499223 NCT03071068	THR-317	PIGF inhibitor	IVT	antibody
DME	NCT01506895	Darapladib	Lipoprotein-associated phospholipase A2 (Lp-PLA2) inhibitor	oral	small molecule
DME	NCT02302079	ASP8232	Vascular adhesion protein-1 (VAP-1) inhibitor	oral	small molecule
DME	NCT02314299	Elamipretide; MTP-131	Cardiolipin peroxidase inhibitor and mitochondria-targeting	eye drop	peptide
DME	NCT02103283	Teprotumumab	IGF-1R antagonist	intravenous infusion	antibody
DME	NCT02002403 NCT01821677	Danazol; DMI-5207	Decreasing blood vessel permeability and the formation of new leaky blood vessels	oral	small molecule
DME	NCT00683176	Choline fenofibrate (SLV348)	PPAR $\alpha$ inhibitor	oral	small molecule
DR	NCT03439345 NCT01927315 NCT01320345	Fenofibrate	PPAR $\alpha$ inhibitor	oral	small molecule
DME; DR	NCT03161652	Levosulpiride	Dopamine D2 receptor blocker	oral	small molecule
DME; RVO	NCT01120899 NCT01468844 NCT01468831	Minocycline	Microglia Inhibitor	oral	small molecule
DME	NCT04292912	GSK2798745	Transient receptor potential vanilloid 4 (TRPV4) channel blocker	oral	small molecule
DR	NCT01726075	Somatostatin; COLIRIOBCN070 660	Inhibiting various hormones and growth factors secretion	eye drop	peptide
DR	NCT03238963	Bi 1467335; PXS 4728A	Aamine oxidase copper-containing 3 (AOCC3) inhibitor	oral	small molecule
DR; ROP	NCT01535495 NCT03038295 NCT03083431 NCT01238471 NCT01079715 NCT02977000 NCT02504944 NCT02014454	Propranolol	$\beta$ 1-adrenergic blocker	oral/eye drop	small molecule
ROP	NCT01660620	Betaxolol	$\beta$ 1-adrenergic antagonist with no partial agonist activity	eye drop	small molecule
DR	NCT00511875	Doxycycline	Anti-inflammation	oral	small molecule
DR	NCT00000159	Sorbinil	Aldose reductase inhibitor	oral	small molecule
DR	NCT03811561	Semaglutide	GLP-1 agonist	subcutaneous injection	small molecule
DR	NCT04283162 NCT01382498	Calcium Dobesilate	Vasoprotective	oral	small molecule
DR	NCT01225653 NCT00619034	Latanoprost	PGF2 analogue	eye drop	small molecule
DR	NCT02753400	Emixustat Hydrochloride; ACU-4429	RPE65 inhibitor	oral	small molecule
RVO	NCT02947867	Aganirsen; GS-101	Inhibiting IRS-1 mRNA expression	eye drop	antisense oligonucleotide
ROP	NCT04191954	Fasudil hydrochloride	Rho-associated coiled coil-forming protein kinase (ROCK) inhibitor	eye drop	small molecule
ROP	NCT01096784 NCT03253263	rhIGF-I/rhIGFBP-3; SHP607; Me casermin rinfabate	IGF-I and IGFBP-3 stimulant	intravenous infusion	protein