STATEMENT ON A NONPROPRIETARY NAME ADOPTED BY THE USAN COUNCIL

USAN (NO-107)	REMIGROMIG
PRONUNCIATION	re mig' roe mig
THERAPEUTIC CLAIM	Treatment of retinal diseases, including diabetic macular edema (DME) and neovascular age related macular degeneration (nAMD)

CHEMICAL NAME

Immunoglobulin G1, trispecific, anti-(human low-density lipoprotein receptor-related protein 5) (human monoclonal IN579/BE298 single-chain variable fragment VH1-(GGGGS)-VL2) fusion protein with peptide linker (synthetic 15-amino acid) fusion protein with immunoglobulin G1 [14-alanine,15-alanine,111-serine,127-methionine,129-phenylalanine,130-aspartic acid,146-tryptophan,148-methionine] (human γ1-chain hinge-CH2-CH3 fragment) fusion protein with peptide linker (synthetic 18-amino acid) fusion protein with immunoglobulin, anti-(human frizzled 4) (human monoclonal LM1222 VH-CH1 domain fragment), (253→249′),(256→252′)-bis(disulfide) with immunoglobulin G1 anti-(human low-density lipoprotein receptor-related protein 5) (human monoclonal BE298/IN579 single-chain variable fragment VH2-(GGGGS)-VL1) fusion protein with peptide linker (synthetic 15-amino acid) fusion protein with immunoglobulin G1 [14-alanine,15-alanine,111-serine,134-isoleucine,137-leucine,140-serine,146-serine,148-alanine,187-valine] (human γ1-chain hinge-CH2-CH3 fragment) fusion protein with peptide linker (synthetic 18-amino acid) fusion protein with immunoglobulin, anti-(human frizzled 4) (human monoclonal LM1222 VH-CH1 domain fragment), disulfide with human monoclonal LM1222 κ-chain

STRUCTURAL FORMULA

Heavy chain knob amino acid sequence:

EVQLVESGGG	LVQPGGSLRL	SCAASGFDFT	AYAMHWVRQA	PGKGLEWVAS	50
IYPSGGYTAY	ADSVKGRFTI	SADTSKNTAY	LQMNSLRAED	TAVYYCARRS	100
YYFALDYWGQ	GTLVTVSSGG	GGSDIQMTQS	PSSLSASVGD	RVTITCRASQ	150
SVSSAVAWYQ	QKPGKAPKLL	IYSASSLYSG	VPSRFSGSRS	GTDFTLTISS	200
LQPEDFATYY	CQQYWAYYSP	ITFGQGTKVE	IKGGGGSGGG	GSEPKSSDKT	250
HTCPPCPAPE	AAGGPSVFLF	PPKPKDTLMI	SRTPEVTCVV	VDVSHEDPEV	300
KFNWYVDGVE	VHNAKTKPRE	EQYNSTYRVV	SVLTVLHQDW	LNGKEYKCKV	350
SNKALPASIE	KTISKAKGQP	REPMVFDLPP	SREEMTKNQV	SLWCMVKGFY	400
PSDIAVEWES	NGQPENNYKT	TPPVLDSDGS	FFLYSKLTVD	KSRWQQGNVF	450
SCSVMHEALH	NHYTQKSLSL	SPGKGGGSGG	GSGGGSGGGS	GSTGEVQLVE	500
SGGGLVQPGG	SLRLSCAASG	FTLSSYSMHW	VRQAPGKGLE	WVAYISSYDS	550
ITDYADSVKG	RFTISADTSK	NTAYLQMNSL	RAEDTAVYYC	ARPAVGHMAF	600
DYWGQGTLVT	VSSASTKGPS	VFPLAPSSKS	TSGGTAALGC	LVKDYFPEPV	650

TVSWNSGALT	SGVHTFPAVL	QSSGLYSLSS	VVTVPSSSLG	TQTYICNVNH	700
KPSNTKVDKK	VEPKSCDKTH	T			721

Heavy chain hole amino acid sequence:

EVQLVESGGG	LVQPGGSLRL	SCAASGFDFS	SSSIHWVRQA	PGKGLEWVAS	50
ISSSYGYTYY	ADSVKGRFTI	SADTSKNTAY	LQMNSLRAED	TAVYYCARSW	100
AMDYWGQGTL	VTVSSGGGGS	DIQMTQSPSS	LSASVGDRVT	ITCRASQSVS	150
SAVAWYQQKP	GKAPKLLIYS	ASDLYSGVPS	RFSGSRSGTD	FTLTISSLQP	200
EDFATYYCQQ	YAGAGLITFG	QGTKVEIKGG	GGSGGGGSEP	KSSDKTHTCP	250
PCPAPEAAGG	PSVFLFPPKP	KDTLMISRTP	EVTCVVVDVS	HEDPEVKFNW	300
YVDGVEVHNA	KTKPREEQYN	STYRVVSVLT	VLHQDWLNGK	EYKCKVSNKA	350
LPASIEKTIS	KAKGQPREPQ	VYTLPPIREL	MTSNQVSLSC	AVKGFYPSDI	400
AVEWESNGQP	ENNYKTTPPV	LDSDGSFFLV	SKLTVDKSRW	QQGNVFSCSV	450
MHEALHNHYT	QKSLSLSPGK	GGGSGGGSGG	GSGGGSGSTG	EVQLVESGGG	500
LVQPGGSLRL	SCAASGFTLS	SYSMHWVRQA	PGKGLEWVAY	ISSYDSITDY	550
ADSVKGRFTI	SADTSKNTAY	LQMNSLRAED	TAVYYCARPA	VGHMAFDYWG	600
QGTLVTVSSA	STKGPSVFPL	APSSKSTSGG	TAALGCLVKD	YFPEPVTVSW	650
NSGALTSGVH	TFPAVLQSSG	LYSLSSVVTV	PSSSLGTQTY	ICNVNHKPSN	700
TKVDKKVEPK	SCDKTHT				717

Light chain amino acid sequence:

DIQMTQSPSS	LSASVGDRVT	ITCRASQSVS	SAVAWYQQKP	GKAPKLLIYS	50
ASSLYSGVPS	RFSGSRSGTD	FTLTISSLQP	EDFATYYCQQ	WYNAPITFGQ	100
GTKVEIKRTV	AAPSVFIFPP	SDEQLKSGTA	SVVCLLNNFY	PREAKVQWKV	150
DNALQSGNSQ	ESVTEQDSKD	STYSLSSTLT	LSKADYEKHK	VYACEVTHQG	200
LSSPVTKSFN	RGEC				214

Disulfide Bridges

- HC-1: C22-HC-1: C96
- HC-1: C146-HC-1: C211
- HC-1: C288-HC-1: C348/HC-2: C284-HC-2: C344
- HC-1: C394-HC-1: C452
- HC-1: C516-HC-1: C590/HC-2: C512-HC-2: C586
- HC-1: C640-HC-1: C696/HC-2: C636-HC-2: C692
- LC: C23-LC: C88
- LC: C134-LC: C194
- HC-2: C22-HC-2: C96
- HC-2: C143-HC-2: C208
- HC-2: C390-HC-2: C448
- HC-1: C253-HC-2: C249 & HC-1: C256-HC-2: C252
- LC: C214-HC-1: C716/LC: C214-HC-2: C712

Terminal Lysine

If the terminal lysine is absent in the heavy chain amino acid sequence, a statement confirming that indeed there is no lysine codon in the nucleotide sequence (if not the lysine should be added in the amino acid sequence mentioning the posttranslational modification clipping).

No N-terminal lysine codons are included in the nucleotide sequence.

Antibody Glycosylation (including location, type of sugar, etc.)

The antibody is heterogeneously N-link glycosylated at Asn324 of the Heavy Chain knob and Asn320 for Heavy Chain hole chains.

MOLECULAR FORMULA	$C_{8812}H_{13568}N_{2370}O_{2812}S_{62}$
MOLECULAR WEIGHT	199.69 kDa
TRADEMARK	None as yet
SPONSOR	Merck Sharp & Dohme LLC
CODE DESIGNATIONS	MK-3000; EYE103
CAS REGISTRY NUMBER	3059389-31-7
UNII	C3TZ3X6VNV
WHO NUMBER	13973

gbk