

June 25, 2014

## STATEMENT ON A NONPROPRIETARY NAME ADOPTED BY THE USAN COUNCIL

USAN (bc-32) ENFORTUMAB VEDOTIN

PRONUNCIATION en fort' ue mab ve doe' tin

THERAPEUTIC CLAIM Treatment of cancers expressing Nectin-4

## CHEMICAL NAMES

1. Immunoglobulin G1 (human monoclonal AGS-22M6  $\gamma$ 1-chain), disulfide with human monoclonal AGS-22M6  $\kappa$ -chain, dimer, tetrakis(thioether) with *N*-[[[4-[[*N*-[6-(3-mercapto-2,5-dioxo-1-pyrrolidinyl)-1-oxohexyl]-L-valyl-*N*<sup>6</sup>-(aminocarbonyl)-L-ornithyl]amino]phenyl]methoxy]carbonyl]-*N*-methyl-L-valyl-*N*-[(1*S*,2*R*)-4-[(2*S*)-2-[(1*R*,2*R*)-3-[(1*R*,2*S*)-2-hydroxy-1-methyl-2-phenylethyl]amino]-1-methoxy-2-methyl-3-oxopropyl]-1-pyrrolidinyl]-2-methoxy-1-[(1*S*)-1-methylpropyl]-4-oxobutyl]-*N*-methyl-L-valinamide
2. Immunoglobulin G1-kappa, anti-(human PVRL4 (poliovirus receptor-related 4, nectin 4)), human monoclonal antibody conjugated to auristatin E:  $\gamma$ 1 heavy chain (1-446) [human VH (IGHV3-48\*02 (98%) –IGHJ6\*01) [8.8.10] (1-117) –IGHG1\*03 des-K<sup>107(CH3)</sup> (118-446)], (220-214')-disulfide with  $\kappa$  light chain (1'-214') [human V-KAPPA (IGKV1D-12\*01 (97%) –IGKJ4\*01) [6.3.9] (1'-107') –IGKC\*03 (108'-214')], dimer (226-226":229-229")-bisdisulfide; some of the interchain disulfide bridges are cleaved and an average of 4 reduced cysteines are *S*-substituted by (3*RS*)-1-[(8*S*,11*S*)-11-[(4-[(5*S*,8*S*,11*S*,12*R*)-14-[(2*S*)-2-[(1*R*,2*R*)-3-[(1*R*,2*S*)-2-hydroxy-1-methyl-2-phenylethyl]amino]-1-methoxy-2-methyl-3-oxopropyl]pyrrolidin-1-yl)-12-methoxy-4,10-dimethyl-5,8-bis(1-methylethyl)-11-[(1*S*)-1-methylpropyl]-3,6,9,14-tetraoxo-2-oxa-4,7,10-triazatetradecyl]phenyl)acetyl]-8-(1-methylethyl)-6,9,16-trioxo-7,10,15,17-tetraazaheptadecyl]-2,5-dioxo-1*H*-pyrrolidin-3-yl radicals

## STRUCTURAL FORMULA

## Heavy chain

<u>E</u> VQLVESGGG	LVQPGGSLRL	SCAASGFTFS	SYNMNWVRQA	PGKGLEWVSY	50
ISSSSSTIYY	ADSVKGRFTI	SRDNAKNSLS	LQMNSLRDED	TAVYYCARAY	100
YYGMDVWGQG	TTVTVSSAST	KGPSVFPLAP	SSKSTSGGTA	ALGCLVKDYF	150
PEPVTVSWNS	GALTSGVHTF	PAVLQSSGLY	SLSSVVTVPS	SSLGTQTYIC	200
NVNHKPSNTK	VDKRVEPKSC	DKTHTC <u>P</u> PCP	APELLGGPSV	FLFPPKPKDT	250
LMSRTP EVT	CVVVDVSHED	PEVKFNWYVD	GVEVHNAKTK	PREEQYNSTY	300
RVVSVLTVLH	QDWLNGKEYK	CKVSNKALPA	PIEKTISKAK	GQPREPQVYT	350
LPPSREEMTK	NQVSLTCLVK	GFYPSDIAVE	WESNGQPENN	YKTPPVLDS	400
DGSFFLYSKL	TVDKSRWQQG	NVFCSCVMHE	ALHNHYTQKS	LSLSPG	446

## Light chain

DIQMTQSPSS	VSASVGRVTV	ITCRASQGIS	GWLAWYQQKP	GKAPKFLIYA	50'
ASTLQSGVPS	RFSGSGSGTD	F <sup>T</sup> LTLSLQ	EDFATYYCQQ	ANSFPPPTFGG	100'
GTKVEIKRTV	AAPSVFIFPP	SDEQLKSGTA	SVVCLLNFFY	PREAKVQWKV	150'
DNALQSGNSQ	ESVTEQDSKD	STYSLSSLT	LSKADYEKHK	VYACEVTHQG	200'
LSSPVTKSFN	RGE <u>C</u>				214'

# ENFORTUMAB VEDOTIN

M14

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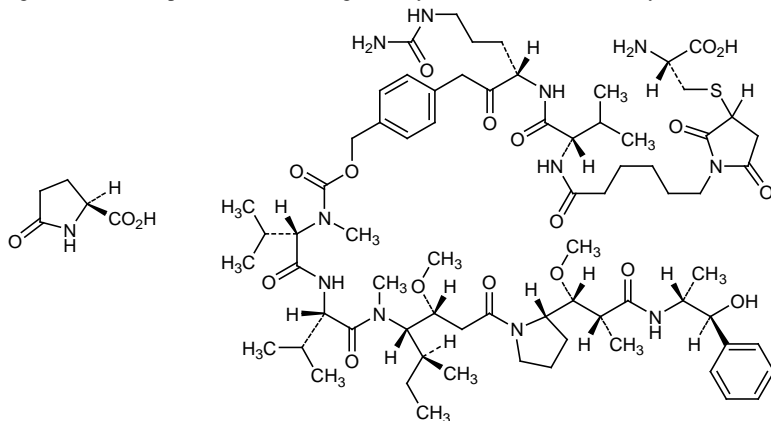
## Disulfide bridges location

22-96	22"-96"	23'-88'	23'''-88'''	134'-194'	134'''-194'''	144-200	144"-200"
214'-220	214'''-220'''	226-226"	229-229"	261-321	261'''-321'''	367-425	367"-425"

## Modified residues

E  
1, 1"  
pyroglutamic acid (Glp)

C  
214', 214"', 220, 220"', 226, 226"', 229, 229"  
an average of 4 cysteines are S substituted by vedotin



MOLECULAR FORMULA

$C_{6642}H_{10284}N_{1742}O_{2063}S_{46}$

MOLECULAR WEIGHT

149.0 kDa

TRADEMARK

None as yet

SPONSOR

Seattle Genetics Inc.

CODE DESIGNATIONS

AGS-22CE, AGS-22ME, AGS-22M6E

CAS REGISTRY NUMBER

1346452-25-2

UNII

DLE8519RWM

WHO NUMBER

9821

gbk