

STATEMENT ON A NONPROPRIETARY NAME ADOPTED BY THE USAN COUNCIL

USAN (HI-209) CINREBAFUSP ALFA  
 PRONUNCIATION sin re' ba fusp al' fa  
 THERAPEUTIC CLAIM Treatment of HER2+ tumors

CHEMICAL NAMES

1. Immunoglobulin G4 [228-proline, 234-alanine, 235-alanine], anti-(human tyrosine kinase receptor HER2) (human-*Mus musculus* monoclonal PRS-343  $\gamma$ 4-chain) fusion protein peptide (synthetic 15-amino acid linker) fusion protein with lipocalin 2 (human mutein), disulfide with human-*Mus musculus* monoclonal PRS-343  $\kappa$ -chain, dimer (CAS)
2. [S<sup>228</sup>>P, F<sup>234</sup>>A, L<sup>235</sup>>A] immunoglobulin G4-kappa (chimeric human-*Mus musculus*, anti-(receptor tyrosine-protein kinase erbB-2, ERBB2, HER2)) fused on both heavy chains (1-447, 1''-447'') via a (G<sub>4</sub>S)<sub>3</sub> linker (448-462, 448''-462'') to a CD137 (tumor necrosis factor receptor superfamily member 9, TNFRSF9, 4-1BB)-targeting mutant (23 exchanged residues) of human lipocalin-2 (neutrophil gelatinase-associated lipocalin, NGAL, oncogene 24p3, siderocalin) (463-640, 463''-640''): gamma4 heavy chain fused to lipocalin-2 mutein (1-640) [*Homo sapiens* VH CH1 CH2 CH3 (*Homo sapiens* IGHV3-66\*01 -(IGHD)- IGHJ4\*01 [CDRKabatH1: DTYIH (31-35); CDRKabatH2: RIYPTNGYTRYADSVKG (50-66); CDRKabatH3: WGGDGFYAMDY (99-109)] (1-120) - *Homo sapiens* IGHG4\*01 (CH1 (121-218), hinge (S<sup>228</sup>>P) (219-230), CH2 (F<sup>234</sup>>A, L<sup>235</sup>>A) (231-340), CH3 (341-445), CHS (446-447)) (1-447) - (G<sub>4</sub>S)<sub>3</sub> linker (448-462) -human lipocalin-2 [mutant Q28>H, L<sup>36</sup>>Q, A<sup>40</sup>>I, I<sup>41</sup>>R, Q<sup>49</sup>>I, Y<sup>52</sup>>M, N<sup>65</sup>>D, S<sup>68</sup>>M, L<sup>70</sup>>K, R<sup>72</sup>>D, K<sup>73</sup>>D, D<sup>77</sup>>M, W<sup>79</sup>>D, R<sup>81</sup>>W, C<sup>87</sup>>S, N<sup>96</sup>>K, Y<sup>100</sup>>F, L<sup>103</sup>>H, Y<sup>106</sup>>S, K<sup>125</sup>>F, S<sup>127</sup>>F, Y<sup>132</sup>>E, K<sup>134</sup>>Y (1-178)] (463-640)], (134-214')-disulfide with kappa light chain (1'- 214') [*Homo sapiens* VL CL (*Homo sapiens* IGKV1-39\*01 -IGKJ1\*01 [CDRKabatL1: RASQDVNTAVA (24'-34'); CDRKabatL2: SASFLYS (50'- 56'); CDRKabatL3: QQHYTTPTPT (89'-97')] (1'-107') - *Homo sapiens* IGKC\*01 (108'-214')]; dimer (226-226''-229-229'')-bisdisulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa (WHO INN list #121)

STRUCTURAL FORMULA

Heavy chain

EVQLVESGGG	LVQPGGSLRL	SCAASGFNIK	DTYIHWVQA	PGKLEWVAR	50
IYPTNGYTRY	ADSVKGRFTI	SADTSKNTAY	LQMNSLRAED	TAVYCSRWG	100
GDGFYAMDYW	GQGTLLTVSS	ASTKGPSVFP	LAPCSRSTSE	STAALGCLVK	150
DYFPEPVTVS	WNSGALTSVG	HTFPAVLQSS	GLYSLSSVVT	VPSSSLGTKT	200
YTCNVDHKPS	NTKVKDRVES	KYGPPCPPCP	APEAAGGPSV	FLFPPKPKDT	250
LMISRTPEVT	CVVVDVSQED	PEVQFNWYVD	GVEVHNAKTK	PREEQFNSTY	300
RVVSVLTVLH	QDWLNGKEYK	KVSVNKGKLP	SIEKISKAK	GQPREPQVYT	350
LPDSQSEEMTK	NQVSLTCLVK	GFYPSDIAVE	WESNGQPENN	YKTTTPPVLDS	400
DGSFFLYSRL	TVDKSRWQEG	NVFSCSVMHE	ALHNHYTQKS	LSLSLGKGGG	450
GGGGGGGGGG	GSQDSTSDLI	PAPPLSKVPL	QQNFQDNQFH	GKWYVVGQAG	500
NIRLREDKDP	IKMMATYIEL	KEDKSYDVTM	VKFDKCKCMY	DIWTFVPGSQ	550
PGEFTLTKIK	SFPFGHTSSLV	RVVSTNYNQH	AMVFFKFFVFQ	NREEFYITLY	600
GRTKELTSEL	KENFIRFSKS	LGLPENHIVF	PVPIDQCIDG		640

Light chain

DIQMTQSPSS	LSASVGRVTV	ITCRASQDVN	TAVAWYQQKP	GKAPKLLIYS	50'
ASFLYSGVPS	RFSGSRSGTD	FTLTISSLQP	EDFATYYCQQ	HYTTPPTFGQ	100'
GTKVEIKRTV	AAPSVFIFPP	SDEQLKSGTA	SVVCLLNNFY	PREAKVQWKV	150'
DNALQSGNSQ	ESVTEQDSKD	STYSLSSTLT	LSKADYKHK	VYACEVTHQG	200'
LSSPVTKSFN	RGEC				214'

Disulfide bridges

22-96	22''-96''	23'-88'	23'''-88'''	134'-194'	134'''-194'''	134-203'	134''-203''
147-203	147''-203''	226-226''	229-229''	261-321	261''-321''	367-426	367''-425''
538-647	538''-647''						

MOLECULAR FORMULA C8364 H12850 N2222 O2592 S58

MOLECULAR WEIGHT 187.9 kDa (reduced)

TRADEMARK None as yet

SPONSOR Pieris Pharmaceuticals, Inc.

CODE DESIGNATIONS PRS-343

CAS REGISTRY NUMBER 2218515-90-1

UNII 21Z359Z1CV

WHO NUMBER 11094

SCS