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(54) Title: TREATMENT OF MUCOPOLYSACCHARIDOSIS I WITH FULLY-HUMAN GLYCOSYLATED HUMAN ALPHA-L-IDURONIDASE (IDUA)

Human Alpha-L-iduronidase (huIDUA)

Signal	Alpha-L-iduronidase
10	30
MRPLRPRAAL LALLASLLAA PPVAPAFAPH IHHVDAARAL WPLRREKST	40
50	70
GFCCPLPHSQ AQYVLSWDQ QNLAYVGVY PARGTKQVRI HALLLELVTR	80
110	120
GSTGRGLSYN FTHLDGYLCL LRENQLLPQF SIMASASGHF TDFEKGQVF	130
160	170
EWKDLVSSLA RRVIGRYGLA HVGKWNPEYH NEPDHHDFFN VSMITAGCPLN	180
210	220
YIDAGSEGLR AASPALRLGG PGSEFHTPPR SPLSGLLLEH CHDGTNFTG	230
260	270
EAGVRLDYIS LHRKGRSSSI SILEQEKVVA QQIRQLPPAF ADFPYIDDA	280
310	320
EPILGWSL EPQ PWRADVTIAR MVVKVIAQHQ NLLLANTTSA FPYALLSDN	330
N-372 req'd for binding & activity	
360	370
AFLSYHPHFY AQRILTAREQ VNTRPPHVC LRRKFLVTAM GLALLLEDEQ	380
410	420
LMAEVSQACT VLDS NPUGV LASAHRQGG AARNTAAVLI YASDCTRAHP	430
460	470
NRSVAVTLEL RGVPMGPGLV YVTRYLQGLD CSPDGEARRL GRPVFFTRAQ	480
Disulfide	
510	520
FRRMRAEDP VAAAPRFLPA GGRILTLRPL RLESILLVHV QARPEKPGQ	530
Bond	
560	570
VTRLRALPLT QGQLVLWSD ENVGSGCLWT YZIQFSQDGK AYTPTVSRPS	580
610	620
TFNLEVFSD TGAVSGSYRV RALDYWARCG PFSQPVYLE VQVPGSPS?	630

GN?

N = N-linked glycosylation site (GlcNac...)
Y = Y-sulfonation site
L = Disulfide Bond

FIG. 1

(57) Abstract: Compositions and methods are described for the delivery of a fully human-glycosylated (HuGly) α -L-iduronidase (IDUA) to the cerebrospinal fluid of the central nervous system (CNS) of a human subject diagnosed with mucopolysaccharidosis I (MPS I).

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