STATEMENT ON A NONPROPRIETARY NAME ADOPTED BY THE USAN COUNCIL

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|---|---|
| USAN (MN-129) | ZICLUMERAN |
| PRONUNCIATION | zye” kloo mer’ an |
| THERAPEUTIC CLAIM | Treatment of transthyretin amyloidosis (ATTR) |

CHEMICAL NAME

RNA (recombinant 5′-(m$^7$Gm-(5′→5′)-ppp-G)-capped all uridine→*N*$^1$-methylpseudouridine-substituted synthetic CRISPR-associated endodeoxyribonuclease CAS9 low codon A-optimized-specifying plus Xenopus laevis β-globin 5′-and 3′-untranslated flanking region-containing poly(A)-tailed messenger)

Messenger RNA (mRNA), 5' capped, encoding codon-optimised clustered regularly interspaced short palindromic repeats (CRISPR) associated protein 9 (Cas9), flanked by untranslated regions (UTR) with significant sequence homology to the *Xenopus* beta globin gene, and terminated with a polyadenylation (polyA) tail. A Kozak sequence precedes the open reading frame and the 5' cap is a synthetic anti-reverse cap analogue (ARCA); contains *N*1-methylpseudouridine instead of uridine (*all*-U>m1Ψ)

**G**GGAAGCUCA GAAUAAACGC UCAACUUUGG CCGGAUCUGC CACCAUGGAC 50
AAGAAGUACU CCAUCGGCCU GGACAUCGGC ACCAACUCCG UGGGCUGGGC 100
CGUGAUCACC GACGAGUACA AGGUGCCCUC CAAGAAGUUC AAGGUGCUGG 150
GCAACACCGA CCGGCACUCC AUCAAGAAGA ACCUGAUCGG CGCCCUGCUG 200
UUCGACUCCG GCGAGACCGC CGAGGCCACC CGGCUGAAGC GGACCGCCCG 250
GCGGCGGUAC ACCCGGCGGA AGAACCGGAU CUGCUACCUG CAGGAGAUCU 300
UCUCCAACGA GAUGGCCAAG GUGGACGACU CCUUCUUCCA CCGGCUGGAG 350
GAGUCCUUCC UGGUGGAGGA GGACAAGAAG CACGAGCGGC ACCCCAUCUU 400
CGGCAACAUC GUGGACGAGG UGGCCUACCA CGAGAAGUAC CCCACCAUCU 450
ACCACCUGCG GAAGAAGCUG GUGGACUCCA CCGACAAGGC CGACCUGCGG 500
CUGAUCUACC UGGCCCUGGC CCACAUGAUC AAGUUCCGGG GCCACUUCCU 550
GAUCGAGGGC GACCUGAACC CCGACAACUC CGACGUGGAC AAGCUGUUCA 600
UCCAGCUGGU GCAGACCUAC AACCAGCUGU UCGAGGAGAA CCCCAUCAAC 650
GCCUCCGGCG UGGACGCCAA GGCCAUCCUG UCCGCCCGGC UGUCCAAGUC 700
CCGGCGGCUG GAGAACCUGA UCGCCCAGCU GCCCGGCGAG AAGAAGAACG 750
GCCUGUUCGG CAACCUGAUC GCCCUGUCCC UGGGCCUGAC CCCCAACUUC 800
AAGUCCAACU UCGACCUGGC CGAGGACGCC AAGCUGCAGC UGUCCAAGGA 850
CACCUACGAC GACGACCUGG ACAACCUGCU GGCCCAGAUC GGCGACCAGU 900
ACGCCGACCU GUUCCUGGCC GCCAAGAACC UGUCCGACGC CAUCCUGCUG 950
UCCGACAUCC UGCGGGUGAA CACCGAGAUC ACCAAGGCCC CCCUGUCCGC 1000
CUCCAUGAUC AAGCGGUACG ACGAGCACCA CCAGGACCUG ACCCUGCUGA 1050
AGGCCCUGGU GCGGCAGCAG CUGCCCGAGA AGUACAAGGA GAUCUUCUUC 1100
GACCAGUCCA AGAACGGCUA CGCCGGCUAC AUCGACGGCG GCGCCUCCCA 1150
GGAGGAGUUC UACAAGUUCA UCAAGCCCAU CCUGGAGAAG AUGGACGGCA 1200
CCGAGGAGCU GCUGGUGAAG CUGAACCGGG AGGACCUGCU GCGGAAGCAG 1250
CGGACCUUCG ACAACGGCUC CAUCCCCCAC CAGAUCCACC UGGGCGAGCU 1300
GCACGCCAUC CUGCGGCGGC AGGAGGACUU CUACCCCUUC CUGAAGGACA 1350
ACCGGGAGAA GAUCGAGAAG AUCCUGACCU UCCGGAUCCC CUACUACGUG 1400
GGCCCCCUGG CCCGGGGCAA CUCCCGGUUC GCCUGGAUGA CCCGGAAGUC 1450
CGAGGAGACC AUCACCCCCU GGAACUUCGA GGAGGUGGUG GACAAGGGCG 1500
CCUCCGCCCA GUCCUUCAUC GAGCGGAUGA CCAACUUCGA CAAGAACCUG 1550
CCCAACGAGA AGGUGCUGCC CAAGCACUCC CUGCUGUACG AGUACUUCAC 1600

CGUGUACAAC GAGCUGACCA AGGUGAAGUA CGUGACCGAG GGCAUGCGGA 1650
AGCCCGCCUU CCUGUCCGGC GAGCAGAAGA AGGCCAUCGU GGACCUGCUG 1700
UUCAAGACCA ACCGGAAGGU GACCGUGAAG CAGCUGAAGG AGGACUACUU 1750
CAAGAAGAUC GAGUGCUUCG ACUCCGUGGA GAUCUCCGGC GUGGAGGACC 1800
GGUUCAACGC CUCCCUGGGC ACCUACCACG ACCUGCUGAA GAUCAUCAAG 1850
GACAAGGACU UCCUGGACAA CGAGGAGAAC GAGGACAUCC UGGAGGACAU 1900
CGUGCUGACC CUGACCCUGU UCGAGGACCG GGAGAUGAUC GAGGAGCGGC 1950
UGAAGACCUA CGCCCACCUG UUCGACGACA AGGUGAUGAA GCAGCUGAAG 2000
CGGCGGCGGU ACACCGGCUG GGGCCGGCUG UCCCGGAAGC UGAUCAACGG 2050
CAUCCGGGAC AAGCAGUCCG GCAAGACCAU CCUGGACUUC CUGAAGUCCG 2100
ACGGCUUCGC CAACCGGAAC UUCAUGCAGC UGAUCCACGA CGACUCCCUG 2150
ACCUUCAAGG AGGACAUCCA GAAGGCCCAG GUGUCCGGCC AGGGCGACUC 2200
CCUGCACGAG CACAUCGCCA ACCUGGCCGG CUCCCCCGCC AUCAAGAAGG 2250
GCAUCCUGCA GACCGUGAAG GUGGUGGACG AGCUGGUGAA GGUGAUGGGC 2300
CGGCACAAGC CCGAGAACAU CGUGAUCGAG AUGGCCCGGG AGAACCAGAC 2350
CACCCAGAAG GGCCAGAAGA ACUCCCGGGA GCGGAUGAAG CGGAUCGAGG 2400
AGGGCAUCAA GGAGCUGGGC UCCCAGAUCC UGAAGGAGCA CCCCGUGGAG 2450
AACACCCAGC UGCAGAACGA GAAGCUGUAC CUGUACUACC UGCAGAACGG 2500
CCGGGACAUG UACGUGGACC AGGAGCUGGA CAUCAACCGG CUGUCCGACU 2550
ACGACGUGGA CCACAUCGUG CCCCAGUCCU UCCUGAAGGA CGACUCCAUC 2600
GACAACAAGG UGCUGACCCG GUCCGACAAG AACCGGGGCA AGUCCGACAA 2650
CGUGCCCUCC GAGGAGGUGG UGAAGAAGAU GAAGAACUAC UGGCGGCAGC 2700
UGCUGAACGC CAAGCUGAUC ACCCAGCGGA AGUUCGACAA CCUGACCAAG 2750
GCCGAGCGGG GCGGCCUGUC CGAGCUGGAC AAGGCCGGCU UCAUCAAGCG 2800
GCAGCUGGUG GAGACCCGGC AGAUCACCAA GCACGUGGCC CAGAUCCUGG 2850
ACUCCCGGAU GAACACCAAG UACGACGAGA ACGACAAGCU GAUCCGGGAG 2900
GUGAAGGUGA UCACCCUGAA GUCCAAGCUG GUGUCCGACU UCCGGAAGGA 2950
CUUCCAGUUC UACAAGGUGC GGGAGAUCAA CAACUACCAC CACGCCCACG 3000
ACGCCUACCU GAACGCCGUG GUGGGCACCG CCCUGAUCAA GAAGUACCCC 3050
AAGCUGGAGU CCGAGUUCGU GUACGGCGAC UACAAGGUGU ACGACGUGCG 3100
GAAGAUGAUC GCCAAGUCCG AGCAGGAGAU CGGCAAGGCC ACCGCCAAGU 3150
ACUUCUUCUA CUCCAACAUC AUGAACUUCU UCAAGACCGA GAUCACCCUG 3200
GCCAACGGCG AGAUCCGGAA GCGGCCCCUG AUCGAGACCA ACGGCGAGAC 3250
CGGCGAGAUC GUGUGGGACA AGGGCCGGGA CUUCGCCACC GUGCGGAAGG 3300
UGCUGUCCAU GCCCCAGGUG AACAUCGUGA AGAAGACCGA GGUGCAGACC 3350
GGCGGCUUCU CCAAGGAGUC CAUCCUGCCC AAGCGGAACU CCGACAAGCU 3400
GAUCGCCCGG AAGAAGGACU GGGACCCCAA GAAGUACGGC GGCUUCGACU 3450
CCCCCACCGU GGCCUACUCC GUGCUGGUGG UGGCCAAGGU GGAGAAGGGC 3500
AAGUCCAAGA AGCUGAAGUC CGUGAAGGAG CUGCUGGGCA UCACCAUCAU 3550
GGAGCGGUCC UCCUUCGAGA AGAACCCCAU CGACUUCCUG GAGGCCAAGG 3600
GCUACAAGGA GGUGAAGAAG GACCUGAUCA UCAAGCUGCC CAAGUACUCC 3650
CUGUUCGAGC UGGAGAACGG CCGGAAGCGG AUGCUGGCCU CCGCCGGCGA 3700
GCUGCAGAAG GGCAACGAGC UGGCCCUGCC CUCCAAGUAC GUGAACUUCC 3750
UGUACCUGGC CUCCCACUAC GAGAAGCUGA AGGGCUCCCC CGAGGACAAC 3800
GAGCAGAAGC AGCUGUUCGU GGAGCAGCAC AAGCACUACC UGGACGAGAU 3850
CAUCGAGCAG AUCUCCGAGU UCUCCAAGCG GGUGAUCCUG GCCGACGCCA 3900
ACCUGGACAA GGUGCUGUCC GCCUACAACA AGCACCGGGA CAAGCCCAUC 3950
CGGGAGCAGG CCGAGAACAU CAUCCACCUG UUCACCCUGA CCAACCUGGG 4000
CGCCCCCGCC GCCUUCAAGU ACUUCGACAC CACCAUCGAC CGGAAGCGGU 4050
ACACCUCCAC CAAGGAGGUG CUGGACGCCA CCCUGAUCCA CCAGUCCAUC 4100
ACCGGCCUGU ACGAGACCCG GAUCGACCUG UCCCAGCUGG GCGGCGACGG 4150
CGGCGGCUCC CCCAAGAAGA AGCGGAAGGU GUGA**CUAGCA CCAGCCUCAA 4200**
**GAACACCCGA AUGGAGUCUC UAAGCUACAU AAUACCAACU UACACUUUAC 4250**
**AAAAUGUUGU CCCCCAAAAU GUAGCCAUUC GUAUCUGCUC CUAAUAAAAA 4300**
**GAAAGUUUCU UCACAUUCUC UCGAG**AAAAA AAAAAAAAAA AAAAAAAAAA 4350
AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA 4400
AAAAAAAAAA AAAAAAAAUC UAG 4423

MOLECULAR FORMULA Not determined

| | |
|---|---|
| MOLECULAR WEIGHT | Not determined |
| TRADEMARK | None as yet |
| SPONSOR | Intellia Therapeutics, Inc. |
| CODE DESIGNATIONS | mRNA000042 (a component of NTLA-2001) |
| CAS REGISTRY NUMBER | 2305431-29-0 |
| UNII | JJ5AS2HL3G |
| WHO NUMBER | 12328 |

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