

6022296PCT ST25  
SEQUENCE LISTING

<110> Amsterdam Molecular Therapeutics (AMT) IP B.V.  
 <120> Alanine-glyoxylate aminotransferase therapeutics  
 <130> P6022296PCT  
 <150> EP09151795.3  
 <151> 2009-01-30  
 <160> 8  
 <170> PatentIn version 3.3  
 <210> 1  
 <211> 1179  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> human AGXT I340M allele (rs4426527)

<220>  
 <221> CDS  
 <222> (1)..(1179)

<400> 1  
 atg gcc tct cac aag ctg ctg gtg acc ccc ccc aag gcc ctg ctc aag 48  
 Met Ala Ser His Lys Leu Leu Val Thr Pro Pro Lys Ala Leu Leu Lys  
 1 5 10 15  
 ccc ctc tcc atc ccc aac cag ctc ctg ctg ggg cct ggt cct tcc aac 96  
 Pro Leu Ser Ile Pro Asn Gln Leu Leu Gly Pro Gly Pro Ser Asn  
 20 25 30  
 ctg cct cct cgc atc atg gca gcc ggg ggg ctg cag atg atc ggg tcc 144  
 Leu Pro Pro Arg Ile Met Ala Ala Gly Gly Leu Gln Met Ile Gly Ser  
 35 40 45  
 atg agc aag gat atg tac cag atc atg gac gag atc aag gaa ggc atc 192  
 Met Ser Lys Asp Met Tyr Gln Ile Met Asp Glu Ile Lys Glu Gly Ile  
 50 55 60  
 cag tac gtg ttc cag acc agg aac cca ctc aca ctg gtc atc tcc ggc 240  
 Gln Tyr Val Phe Gln Thr Arg Asn Pro Leu Thr Leu Val Ile Ser Gly  
 65 70 75 80  
 tcg gga cac tgt gcc ctg gag gcc gcc ctg gtc aat gtg ctg gag cct 288  
 Ser Gly His Cys Ala Leu Glu Ala Ala Leu Val Asn Val Leu Glu Pro  
 85 90 95  
 ggg gac tcc ttc ctg gtt ggg gcc aat ggc att tgg ggg cag cga gcc 336  
 Gly Asp Ser Phe Leu Val Gly Ala Asn Gly Ile Trp Gly Gln Arg Ala  
 100 105 110  
 gtg gac atc ggg gag cgc ata gga gcc cga gtg cac ccg atg acc aag 384  
 Val Asp Ile Gly Glu Arg Ile Gly Ala Arg Val His Pro Met Thr Lys  
 115 120 125  
 gac ccc gga ggc cac tac aca ctg cag gag gtg gag gag ggc ctg gcc 432  
 Asp Pro Gly Gly His Tyr Thr Leu Gln Glu Val Glu Glu Gly Leu Ala  
 130 135 140  
 cag cac aag cca gtg ctg ctg ttc tta acc cac ggg gag tcg tcc acc 480  
 Gln His Lys Pro Val Leu Leu Phe Leu Thr His Gly Glu Ser Ser Thr  
 145 150 155 160

## 6022296PCT ST25

ggc	gtg	ctg	cag	ccc	ctt	gat	ggc	ttc	ggg	gaa	ctc	tgc	cac	agg	tac	528
Gly	Val	Leu	Gln	Pro	Leu	Asp	Gly	Phe	Gly	Glu	Leu	Cys	His	Arg	Tyr	
				165					170					175		
aag	tgc	ctg	ctc	ctg	gtg	gat	tcg	gtg	gca	tcc	ctg	ggc	ggg	acc	ccc	576
Lys	Cys	Leu	Leu	Leu	Val	Asp	Ser	Val	Ala	Ser	Leu	Gly	Gly	Thr	Pro	
			180					185					190			
ctt	tac	atg	gac	cgg	caa	ggc	atc	gac	atc	ctg	tac	tcg	ggc	tcc	cag	624
Leu	Tyr	Met	Asp	Arg	Gln	Gly	Ile	Asp	Ile	Leu	Tyr	Ser	Gly	Ser	Gln	
		195					200					205				
aag	gcc	ctg	aac	gcc	cct	cca	ggg	acc	tcg	ctc	atc	tcc	ttc	agt	gac	672
Lys	Ala	Leu	Asn	Ala	Pro	Pro	Gly	Thr	Ser	Leu	Ile	Ser	Phe	Ser	Asp	
	210					215					220					
aag	gcc	aaa	aag	aag	atg	tac	tcc	cgc	aag	acg	aag	ccc	ttc	tcc	ttc	720
Lys	Ala	Lys	Lys	Lys	Met	Tyr	Ser	Arg	Lys	Thr	Lys	Pro	Phe	Ser	Phe	
	225				230					235					240	
tac	ctg	gac	atc	aag	tgg	ctg	gcc	aac	ttc	tgg	ggc	tgt	gac	gac	cag	768
Tyr	Leu	Asp	Ile	Lys	Trp	Leu	Ala	Asn	Phe	Trp	Gly	Cys	Asp	Asp	Gln	
				245					250					255		
ccc	agg	atg	tac	cat	cac	aca	atc	ccc	gtc	atc	agc	ctg	tac	agc	ctg	816
Pro	Arg	Met	Tyr	His	His	Thr	Ile	Pro	Val	Ile	Ser	Leu	Tyr	Ser	Leu	
			260					265					270			
aga	gag	agc	ctg	gcc	ctc	att	gcg	gaa	cag	ggc	ctg	gag	aac	agc	tgg	864
Arg	Glu	Ser	Leu	Ala	Leu	Ile	Ala	Glu	Gln	Gly	Leu	Glu	Asn	Ser	Trp	
		275					280					285				
cgc	cag	cac	cgc	gag	gcc	gcg	gcg	tat	ctg	cat	ggg	cgc	ctg	cag	gca	912
Arg	Gln	His	Arg	Glu	Ala	Ala	Ala	Tyr	Leu	His	Gly	Arg	Leu	Gln	Ala	
	290				295						300					
ctg	ggg	ctg	cag	ctc	ttc	gtg	aag	gac	ccg	gcg	ctc	cgg	ctt	ccc	aca	960
Leu	Gly	Leu	Gln	Leu	Phe	Val	Lys	Asp	Pro	Ala	Leu	Arg	Leu	Pro	Thr	
	305				310					315					320	
gtc	acc	act	gtg	gct	gta	ccc	gct	ggc	tat	gac	tgg	aga	gac	atc	gtc	1008
Val	Thr	Thr	Val	Ala	Val	Pro	Ala	Gly	Tyr	Asp	Trp	Arg	Asp	Ile	Val	
				325					330					335		
agc	tac	gtc	atg	gac	cac	ttc	gac	att	gag	atc	atg	ggg	ggc	ctt	ggg	1056
Ser	Tyr	Val	Met	Asp	His	Phe	Asp	Ile	Glu	Ile	Met	Gly	Gly	Leu	Gly	
			340					345					350			
ccc	tcc	acg	ggg	aag	gtg	ctg	cgg	atc	ggc	ctg	ctg	ggc	tgc	aat	gcc	1104
Pro	Ser	Thr	Gly	Lys	Val	Leu	Arg	Ile	Gly	Leu	Leu	Gly	Cys	Asn	Ala	
		355					360					365				
acc	cgc	gag	aat	gtg	gac	cgc	gtg	acg	gag	gcc	ctg	agg	gcg	gcc	ctg	1152
Thr	Arg	Glu	Asn	Val	Asp	Arg	Val	Thr	Glu	Ala	Leu	Arg	Ala	Ala	Leu	
	370					375					380					
cag	cac	tgc	ccc	aag	aag	aag	ctg	tga								1179
Gln	His	Cys	Pro	Lys	Lys	Lys	Leu									
					390											

<210> 2  
 <211> 392  
 <212> PRT  
 <213> Homo sapiens

<400> 2

6022296PCT ST25

Met Ala Ser His Lys Leu Leu Val Thr Pro Pro Lys Ala Leu Lys  
1 5 10 15

Pro Leu Ser Ile Pro Asn Gln Leu Leu Gly Pro Gly Pro Ser Asn  
20 25 30

Leu Pro Pro Arg Ile Met Ala Ala Gly Gly Leu Gln Met Ile Gly Ser  
35 40 45

Met Ser Lys Asp Met Tyr Gln Ile Met Asp Glu Ile Lys Glu Gly Ile  
50 55 60

Gln Tyr Val Phe Gln Thr Arg Asn Pro Leu Thr Leu Val Ile Ser Gly  
65 70 75 80

Ser Gly His Cys Ala Leu Glu Ala Ala Leu Val Asn Val Leu Glu Pro  
85 90 95

Gly Asp Ser Phe Leu Val Gly Ala Asn Gly Ile Trp Gly Gln Arg Ala  
100 105 110

Val Asp Ile Gly Glu Arg Ile Gly Ala Arg Val His Pro Met Thr Lys  
115 120 125

Asp Pro Gly Gly His Tyr Thr Leu Gln Glu Val Glu Glu Gly Leu Ala  
130 135 140

Gln His Lys Pro Val Leu Leu Phe Leu Thr His Gly Glu Ser Ser Thr  
145 150 155 160

Gly Val Leu Gln Pro Leu Asp Gly Phe Gly Glu Leu Cys His Arg Tyr  
165 170 175

Lys Cys Leu Leu Leu Val Asp Ser Val Ala Ser Leu Gly Gly Thr Pro  
180 185 190

Leu Tyr Met Asp Arg Gln Gly Ile Asp Ile Leu Tyr Ser Gly Ser Gln  
195 200 205

Lys Ala Leu Asn Ala Pro Pro Gly Thr Ser Leu Ile Ser Phe Ser Asp  
210 215 220

Lys Ala Lys Lys Lys Met Tyr Ser Arg Lys Thr Lys Pro Phe Ser Phe  
225 230 235 240

Tyr Leu Asp Ile Lys Trp Leu Ala Asn Phe Trp Gly Cys Asp Asp Gln  
245 250 255

Pro Arg Met Tyr His His Thr Ile Pro Val Ile Ser Leu Tyr Ser Leu  
260 265 270

Arg Glu Ser Leu Ala Leu Ile Ala Glu Gln Gly Leu Glu Asn Ser Trp

275 280 6022296PCT ST25 285

Arg Gln His Arg Glu Ala Ala Ala Tyr Leu His Gly Arg Leu Gln Ala  
290 295 300

Leu Gly Leu Gln Leu Phe Val Lys Asp Pro Ala Leu Arg Leu Pro Thr  
305 310 315 320

Val Thr Thr Val Ala Val Pro Ala Gly Tyr Asp Trp Arg Asp Ile Val  
325 330 335

Ser Tyr Val Met Asp His Phe Asp Ile Glu Ile Met Gly Gly Leu Gly  
340 345 350

Pro Ser Thr Gly Lys Val Leu Arg Ile Gly Leu Leu Gly Cys Asn Ala  
355 360 365

Thr Arg Glu Asn Val Asp Arg Val Thr Glu Ala Leu Arg Ala Ala Leu  
370 375 380

Gln His Cys Pro Lys Lys Lys Leu  
385 390

<210> 3  
<211> 673  
<212> DNA  
<213> Artificial

<220>  
<223> Human AAT promoter combined with the mouse albumin gene enhancer  
(Ea1b) element

<400> 3  
tcgaggttcc tagattacac tacacattct gcaagcatag cacagagcaa tgttctactt 60  
taattacttt cattttcttg tatcctcaca gcctagaaaa taacctgcgt tacagcatcc 120  
actcagtatc ccttgagcat gaggtgacac tacttaacat agggacgaga tggtagctttg 180  
tgtctcctgc tctgtcagca gggcacagta cttgctgata ccagggaatg tttgtttctta 240  
aataccatca ttccggacgt gtttgccttg gccagttttc catgtacatg cagaaagaag 300  
tttggactga tcaatacagt cctctgcctt taaagcaata ggaaaaggcc aacttgtcta 360  
cgtttagtat gtggctgtag atctgtaccc gccacccctt ccaccttgga cacaggacgc 420  
tgtggtttct gagccaggta caatgactcc tttcggttaag tgcagtggaa gctgtacact 480  
gcccaggcaa agcgtccggg cagcgtaggc gggcgactca gatcccagcc agtggactta 540  
gcccctgttt gtcctccga taactggggt gaccttggtt aatattcacc agcagcctcc 600  
cccgttgccc ctctggatcc actgcttaaa tacggacgag gacagggccc tgtctcctca 660  
gcttcaggca cca 673

<210> 4  
<211> 96  
<212> DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 4

tccgtcgacc cgggcggccg atcgctagcc tttgaatgta accaatccta ctaataaacc 60

agttctgaag gtgttgtgtg tgcgcgtgtg gagttg 96

&lt;210&gt; 5

&lt;211&gt; 66

&lt;212&gt; DNA

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; Synthetic polyA Insulator

&lt;400&gt; 5

aattcaataa agagctctta ttttcattct cgaggtgtgg ttggttttct tgtgtggggg 60

cggatc 66

&lt;210&gt; 6

&lt;211&gt; 10

&lt;212&gt; RNA

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; Kozak consensus sequence

&lt;400&gt; 6

gccrccaugg 10

&lt;210&gt; 7

&lt;211&gt; 145

&lt;212&gt; DNA

&lt;213&gt; adeno-associated virus 2

&lt;400&gt; 7

ttggccactc cctctctgcg cgctcgctcg ctactgagg ccgggcgacc aaaggtcgcc 60

cgagcggcgg gctttgcccg ggcggcctca gtgagcgagc gagcgcgag agagggagtg 120

gccaactcca tcactagggg ttcct 145

&lt;210&gt; 8

&lt;211&gt; 146

&lt;212&gt; DNA

&lt;213&gt; adeno-associated virus 2

&lt;400&gt; 8

ttggccactc cctctctgcg cgctcgctcg ctactgagg ccggcgggc aaagccggg 60

cgtcgggcca ctttggtcg ccggcctca gtgagcgagc gagcgcgag agagggagtg 120

gccaactcca tcactagggg ttcccc 146