I PIELIKUMS

\   W"**CRTCMUVU**

™ o"| n o"vkgm"rkgo tqvc"rcrknfw"w|tcwf| dc0"V f l fk"d u"kgur lco" vtk"kfgpvkhke v"lcwp mq" kphqto eklw"rct+-q"| w"ftq-wow0"Xgugn dcu"crt rgu"urgek nkuvk"vkgm"n ivk"|k qv"rct"lgdm f o" kgur lco o"pgx nco o"dncmwurct f d o0"Umcv v"60:0 crcm-rwpmvw"rct"vq.m "|k qv"rct"pgx nco o" dncmwurct f d o0

1.   \   W"PQUCWMWOU

NYXTHRACIS 100 o i l o n"mqpegpvt vu"kph |klw"- fwoc"rcicvcxq-cpck

2.   MXCNKVCV XCKU"WP"MXCPVKVCV XCKU"UCUV XU

Mcvtu" o n"mqpegpvt vc"ucvwt"322 o i"qdknvqmucmuk o cdc *(obiltoxaximab)*0"
Xkgpu"8 o n"hncmqpu"ucvwt"822 o i"qdknvqmucmuk o cdc0

Qdknvqmucmuk o cdw"kgi u"rg   w"FU2"okgn o cu"- p u."k| o cpvqlqv"tgeq o dkpcpvq"FPU"vgjpqnq klw0

Rcn ixkgnc"ct"|kp o w"kgfctd dw

Mcvtu" o n"mqpegpvt vc"ucvwt"58 o i"uqtd vc0

Rknpw"rcn ixkgnw"uctcmuvu"umcv v"8030 crcm-rwpmv 0

3.   \   W"HQTOC

Mqpegpvt vu"kph |klw"- fwoc"rcicvcxq-cpck"*uvgtknu"mqpegpvt vu+""
NYXTHRACIS kt"f|kfktu"n f|"qrcnguegpvu."dg|mt uckpu"n f"ick-k"|gnvgpuick-k"dt   picpk"f|gnvgpu"- fwou."mwt-"xct"ucvwt t"fcflcu"ecwtup f igcu"n f|"dcnvcu"rctqte pa"fc k   cu"*mcu"vkmu"cvdclcu"ct"n pklcu" hknvtc"rcn f| dw+"wp"mwtc"r J"n o gpku"kt"7.7"wp"qu o qncnkt vg"499-30: o Quo lmi0

4.   MN PKUM "KPHQTO EKC

4.1. Vgtcrgkvkum u"kpfkm eklcu

NYXTHRACIS kt"kpfke vu"nkgvq-cpck"mqodkp ekl "ct"rgo tqvgo "cpvkdcmvgtk nkgo "n f|gm   kgo"xku u"xgewo c"itwp u"*Bacillus anthracis* kggnrq-cpcu"k|tckus vc"Ukd tklcu"o tc tuv -cpck"*umcv v" 7030 crcm-rwpmvw+0

NYXTHRACIS kt"kpfke vu"rtqhkncmvkumcl"nkgvq-cpck"xku u"xgewo c"itwp u"r e"Ukd tklcu"o tck|tcku t lc" kggnrq-cpcu."mcf"cnvgtpcvkxk u tv -cpcun f|gm   kp cv"rkgo tqvk"xck"pcv"rkgglco k"*umcv v" 7030 crcm-rwpmvw+0

4.2. Fgxcu"wp"nkgvq-cpcu"xgkfu

NYXTHRACIS l nkgvq."vkmn f|v u"kt"mk pkumk"kpfke vcu0

Cpchkncmvkumc"pqvkmwo c"if lwo "r e"*NYXTHRACIS* nkgvq-cpcu"xkgp o t"l d   v"xkgink"rkgglco ck"o gfke pkumck tuv -cpck"wp"w|tcwf| dck0

Fgxcu

Kgvgkeco "*NYXTHRACIS* fgxc"rkgecwiw-kgo "rcekgpvkgo ."mcs"uxgt"xkuo c|"62 mi."kt"xkgpc"kpvtcxgpq|c" kph |klc."kgxcfqv"38"| w"w |"mi" gtog   c"o cucu0"Kgv *NYXTHRACIS* fgxc"rkgecwiw-kgo"

rcekgpvkgo."mcu"uxgt"oc| m"rcr"62 mi."kt"xkgpc"kpvtcxgpq|c"kph |klc."kgxcfqv"46 o i"| w"w|"mi" gt og   c ocucu0"

Rktou"*NYXTHRACIS* kgxcf –cpcu"kgvgkecoc"rtgogfkm eklc"ct"cpvkjkuvo pc"n f|gmnk"*umcv v"6060"wp" 60:0 crcm-rwpmvw+0"

Kphqto eklw"rct"fgxcu"rkgn iq-cpw"ct"kph |klw"uckuv vw"tgcmeklw"*KUT+"icf lwo "umcv v"30 vcdwn 0

1. vcdwnc0"Qdknvqmucmuk o cdc"fgxcu"rkgn iq-cpc"ct"kph |klw"uckuv vw"tgcmeklw"f

KUT"u o c iwo c"rcm rg"	Fgxcu"rkgn iq-cpc
30–50 rcm rgu ct"kph |klw" uckuv vc"tgcmeklc	Qdknvqmucmuk o cdc"kph |klc"kt"l r tvtcwe"wp"l nkgvq"dcnuvvgtcklc0 Rktocl "tgk| ."mcf"pqv tq"50 rcm rgu"s m-cpw."dtqpjqurc| o cu"xkur t lw" p vtgpk."qdknvqmucmuk o cdc"nkgvq-cpc"kt"rknp d "l r tvtcwe0 Cvm tvqlqvkgu"40 rcm rgu"s m-cpck"xck"p vtgpk"xck"cvm tvqlqvkgu"lgdm fkg o" 50 rcm rgu"uk o rvq okg o."qdknvqmucmuk o cdc"nkgvq-cpc"kt"rknp d "l r tvtcwe0" Ekvqu"icf lwo qu"r c"rkgn icu"uk o rvq o"k||w-cpcu"kph |klw"xct"cvu mt"ct"72pq" kph |klcu" tvtcwm."mcu"ucupkgivu"rktou"r tvcwmwo0"Lc"pcx"ct"kph |klw"uckuv vw" uk o rvq ow."rkg o tqlo cki"kph |klcu" tvtcwm kr"ct"rtcmcuv vw"50wn 0 L xgie"rtg o gfkm eklc0
60 rcm rgu ct"kph |klw" uckuv vc"tgcmeklc	Qdknvqmucmuk o cdc"kph |klc"pgmcv lqvkgu"l r tvtcwe0 L nkgvq"dcnuvvgtcklc0 Rknp d "l r tvtcwe"qdknvqmucmuk o cdc"nkgvq-cpc0"

 rc-cu"rqrwn eklcu

I cfqu"xge mk"eknx mk

Fgxcu"rkgn iq-cpc"rcekgpvkgo."mcu"kt × 87 icfwu"xgek."pcv"pgrkgekg-c o c"*umcv v"7040 crcm-rwpmvw+0

Rgfkcvtkum "rqrwn eklc

Rgfkcvtkumkg o "rcekgpvkg"kgvgkeco "fgxc"kt"cvmct ic"pq gt og c" o cucu."m "pqr f vs"l m"40 vcdwn 0

2. vcdwnc0"Kgvgkeco "rgfkcvtkum "qdknvqmucmuk o cdc"fgxc"*cvbknuvq-k" gt og   c" o ouck

gt og c" o cuc"*mi+	Fgxc"*o ilmi" gt og c o cucu)
@ 62	38
> 37"i f|"62	46
37"xck"o c| m	54

Nkgvq-cpcu"xgkfu"

Qdknvqmucmuk o cdu"kt"l kgxcfc";2 okp -w"knicu"kpvtcxgpq|cu"kph |klcu"xgkf 0

Rkguctf| dcu"rcu mwok"rktou"| w"nkgvq-cpcu"xck"t mq-cp u"ct"v o

Hncmqpw"pgff muv"mtcv v0"Rktou"kpvtcxgpq|cu"kph |klcu"qdknvqmucmuk o cdu"l cv- ckfc"p vtklc"jnqt fc" ; oilon"*2.; '+"- fwo "kplgmekl o "*umcv v"8080 crcm-rwpmvw+0

Cv- ckf v "qdknvqmucmuk o cdc"kpvtcxgpq| "kph |klc"l kgxcfc"o 2p -w"nckm "ct" vtwo u." o cu"crtcmuv vu" 50 vcdwn ."k| o cpvqv"kph |klcu" o cikw"xck"kph |klcu"- ktek"kph   w"n pklcu"hknvtw0

Xkucu"kph |klcu"nckm "wp"xkuom|"xkgpw"uvwpfw"r e"| w"kgxcfcuécekgpv"kt r ik"l w|tcwic."nck"
mqpuvcv vw"jkrgtugpukvkxv vgu"rc| om u"wp"ukom rvqomu"*ucmcv t"6040 crcm-rwpmv+0"Ct"kph |klw"uckuv vcu"
tgcmeklcu"l mqpvtqn ."m "pqt f vu"30 vcdwn 0

Kpvtcxgpq| u"kph |klcu"dgki u"l pklc"l k|ucmcq."k mcpvqlqv"p vtklc"jnqt fc"; m nn "*2.; '+- fwow"
kplgmel m0

**3. vcdwnc0"Qdknvqmucmukom cdc"fgxc."mqr lcku"kph |klcu"crlqomu"wp"kph |klcu" vtwom"cvdknuvq-k"
gtomg c"omcuck**

gtomgc"omcuc *mi+ *fgxc"cvdknuvq-k" gtomg omcki)	Mqrlcku"kph |klcu" crlqomu"*oml+ *kph |klcu omckuu"vck" - kteg+,	Kph |klcu" vtwom *oml+
> 40 mi"xck"rkgcwiw-cku"*38 omilmi" gtomg omcuc)		
@"62	472	389
Pq"@"37 mi"l f |"62 mi"*46 omilmi" gtomg omcuc)		
pq"53"l f |"62	472	389
pq"38"l f |"52	100	89
37 mi"xck"om| m"*54 omilmi" gtomg omcuc)		
pq"33"l f |"37	100	89
pq"7"l f |"32	72	55.5
pq"5.3"l f |"6.;	47	39
pq"4.3"l f |"5	42	35.5
pq"3.3"l f |"4	37	10
3"xck"om| m	9	6.9

, Kgvgkmwomus"rct| w"cv- ckf -cpw"rkroml"nkgvq-cpau"wp"kph |klcu"omckuc"xck- ktegs"k| mcpvq-cpw"ucmcv t"
8080 crcm-rwpmv 0

4.3.   Mqpvtkpfkm eklcu

Rccwiuvkp vc"lwv dc"rtgv"cmcv xq"xkgnw"xck"lgdmwtu"pq"8030 crcm-rwpmv "w|umcki vcl m"rcn ixkgn m0

4.4.   rc-k"dt fkp lwomk"wp"rkguctf| dc"nkgvq-cp

Kumgmqlcom dc

Ncki w"|ncdqvwt"dkqnq kumq"| m   w"k|umgmqlcom dwmkokt"ftk"l tg kuvt "nkgvqtq | pqucwmuomu"wp"u tklcu"
pwomwtu0

Ct"kph |klw"uckuv vcu"tgcmeklcom cwiuvkp vc"lwv dc wp"cpchknncmug

Qdknvqmucmukom cdc"mk pkumclqs"r v lwomqs"ct"xgugn om"r v m m"rgtuqp m"dkgfkl"pqx tqlc"ct"kph |klw"
uckuv vcuj ccwiuvkp vcs"lwv dcs tgcmeklcu0Uomciw"tgcmeklw"xck"cpchknncmugu"tkumc d   qdknvqmucmukom cdu"
l kgxcfc"v fc"rgtuqp nc"w|tcwf b ."mcs kt"cr om e vs"wp"mcom ir kgp c is"crt mqlwomus"cpchknncmugs"
mqpvtqngk"Kph |klcu"nckm wp"xkuom|"xkgpw"uvwpfw"r e| w"kgxcd -cpcu"rcekgpvk r   t pkkxlcé|

V "m "nn pkumqs"r v lwomwu"xgkec"ct"xgugnkim "dt vrt v iciqkgm."qdknvqmucmukom cdc"kph |klcu"vkkc"cvtwt vcu"
lgdm fcu"tgcmeklcu"tc-cp s"dt f 0"Dcnuvqtgs"w|"rkgtgd|k"ct"ckt om e vs"wp"mcom ir kgp c is"mq|k| mcpvq"
uomciw"unkom dw"ntu tr -cp ."kph |klcu"rct om vt"rcdgik."lc v"uvkgm"cvdknuvq-k"ttu vcu0"Ct"kph |klw"uckuv vcu"
tgcmeklcu"l mqpvtqn ."m "pqt f vu"30 vcdwn 0

Rktom qdknvqmucmukom cdc"nkgvq-cpcu"igvgkecom s"xgkkm "rtgomfkm eklw"ct"cpvkjkuvcom nc" f|gk igm."
rkgom tcom."fkhgpjkftcom pw"*ucmcv t"6040 crcm-rwpmv+0Qdknvqmucmukom cdc"nn pkumclqs"r v lwomqs"
fkhgpjkftcom pw"nkgvqlc"52 omkp vgu"rktom s" ttu -cpcu"ct"qdknvqmucmukom cdw0"Rtgomfkm ekle ct"
cpvkjkuvcom nc"f|gk   kgom"pgpqx t-"cpchknncmuki"wp"xct"crn pt"xck"ckz|om| camwiuvkp vcu"lwv dcs"
ukom rqomw"tc-cpqs0

4

Ukd tklcu o tc"ogpkpi vu

Qdknvqmucmuk o cdu"pg–   tuq"jg o cvqgpeghcn vkumq"dctlgtw."m "ct "pgpqx t–"wp"pg tuv "Ukd tklcu"o tc" o gpki vw0"

Rgfkcvtkum "rqrwn eklc

Pcx"xgkmvk"qdknvqmucmuk o cdc"ftq–w o c"xck"hct o cmqmkp vkmcu"r v lwo k"rgfkcvtkumcl "rqrwn eki "*umcv v" 7040 crcm–rwpmvw+0

Oklkgfcvtd dcu"ncdqtcvqtklcu"vguvw"nckm

Ucumctg"ct"NYXTHRACIS xct"kgvgm o v"Ukd tklcu"o tc"ugtqnq kumq"vguvw"xgkm–cpw0

Uqtd vu

Mcvtu"NYXTHRACIS o n"ucvwt"58 o i"uqtd vc"*umcv v"40"wp"8030 crcm–rwpmvw+0"
Uqtd vw"ucvwtq–cu| ngu"xct"d v"p x lq–cu."lc v s"kpvtcxgpq|k"kgxcfc"r v o o"rgtuqp o ct"kgf|k o vu" htwmkq|gu"pgrcpguc o dw"*KHP+0"Qdknvqmucmuk o cdw"pgft muv"kngqv"r v o o"rgtuqp o ct"KHP."lc"xkgp" pcx"r tnkgckpq–cu"mk pkumcu"xclcf| dcu"wp"lc"pcx"rkgglc o cu"cnvgrtpcx xcu0"Rktmu–q| w"iklcu–cpq mcvtc"rcekgpvc|l kgx e"fgvcnk| vc"cpcm o |g cvwkge d "w |"KHP"uk o rvq o kgo 0"

\ fck kg o "wp"o c|kg o "d tpkg o "*n f|"4 icfw"xgecmco +"kt" rc–k"cwiuvu"tkumu."lq"xk kg o "xct v x n"pgd v" pqvgkmvc"KHP"fkcipq|g0"

P vtklu

™ u"| ngu"ucvwtu"o c| m"rct"3 o oqn"p vtklc"*45 o i+cvt "8 o n"hncmqp — d v d "v u"kr"šp vklw" pgucvwtq–cuö0"

6070   Oklkgfcvtd dc"ct"ckv o | n o "wp"ckv"oklkgfcvtd dcu"xgkfk

Ekrtqhnqmuce pu

Oklkgfcvtd dcu"r v lwo "62 r v o o "rgtuqp o "cvugxk– k"xck"mqr "ct"ekrtqhnqmuce pw"kgxcf lc"xkgpw" qdknvqmucmuk o cdc"fgxw0"Fkxfgu o kv"r v o u"rgtuqpcu"uc   o c"vkmck"qdknvqmucmuk o cdw."wp e42cu" r v o o "rgtuqpcu"; fkgpcu"uc   o c"qdknvqmucmuk o cdw"mqr "ct"ekrtqhnqmuce pw0"Nkgvqlqv"38lmi" qdknvqmucmuk o cdc"kpvtcxgpq|cu"kph |lkcu"xgkf "rktou"ekrtqhnqmuce pc"kpvtcvgpq|k"kph |lkcu"xck" ekrtqhnqmuce pc"kgm– ik"kgvqlqo cu"cdngvgu"kg o o–cpcu"fkxcu tgk|gu"fkp ."qdknvqmucmuk o cdc" hct o cmqmkp vkc"pg kgm | u0"Qdknvqmucmuk o cdu"ct "pgkgvgm o v lc"kgm– ik"xck"kpvtcvgpq|k"xgkf vc" ekrtqhnqmuce pc"hct o cmqmkp vkw0"

Ekvk"oklkgfcvtd dcu"r v lwo k"pcx"xgkmvk0"V k "qdknvqmucmuk o cdu"kt o qpqmnqp nc"cpvkvkgnc."oklkgfcvtd dcu" tkumu"kt"pgnkgnu0"

608.   Hgtvknkv vg."it   vpkge dc"wp"dctq–cpc"ct"mt   vk

I t   vpkge dc

Pcx"fcvw"rct"qdknvqmucmuk o cdc"nkgvq–cpw"it vpkge o."vq o t"|kp o u."mc"ceknx mc"Ki I "–   tuq"rncegpv tq" dctlgtw0"
R v lwo k"ct"f| xpkgmkg o "pgw|t dc"vkg–w"xck"pgvkg–w"mckv iw"kgvgm o k"ucktu b "ct"tgrtqfwmv xq"vqmukekv vk" *umcv v"7050 crcm–rwpmvw+0"
Rkguctf| dcu"pqn m "x nc o u"k|xckt vkgu"pq"NYXTHRACIS nkgvq–cpcu"it   vpkge dcu"nckm 0"

Dctq-cpc"ct"mt_vk

Pcx"|kp ou."xck"qdknvqmucmukocdu"k|fcn u"o vgu"rkgcp 0"Kt"|kp ou."mc"eknx kc"Ki I"k|fcn u"o vgu"rkgcp "rktocj u"fkgcp u"r e"f|ko-cpcu."wp"r e"vcvo"uvtcwjk"v "fcwf|wou"scocc"kp u"n f|"|gocj"mqpecgpvt eklck0"V r e"-cj " acj "rgtkqf "pgxcat"k|un gv"tkumw"ct"mt vk"dctqvkgo"| fck kgo0"X n k"qdknvqmucmukocdc" nkgvq-pw"xcf"crux vt"| f -cpcu"rgtkqf ."dgv"vkmcc"vcf."lc"vcu"nk pkuki"pgrkgekg-cou0

Hgtvknkv vg

Hgtvknkv vgu"r v lwok"ct"qdknvqmucmukocdw"pcx"xgkkvk0

4.7.   Kgvgmog o g"w|"ur lw"xcf v"vtcpurqtvln f|gm   wu"wp"crmcnrqv"o gj pkuo wu

Qdknvqmucmukocdu"xct"pgpgz o gik"kgvgmog v"ur lw"xcf v"vtcpurqtvln f|gm   wu"wp"crmcnrqv"o gj pkuo wu."lq r e"*NYXTHRACIS nkgvq-pcu"xct"d v"icnxcuu rgu."tgkdqpku."pqiwtuo wu"xge-cpcu "umcv v 60:0 crcm-rwpmvt+0

4.8.   Pgx nc o u"dncmwurct f dcu

Ftq-wo c"rtqhknkc"mqprucxknmwou

Qdknvqmucmukocdc"ftq-wou"kr v vu"vkmck"xgugn o"rkgcwiw- o"r v ocj o"rgtuqp o0

Qdknvqmucmukocdc" ftq-wow" pqx tv lc" 542 xgugn o" r v ocj o" rgtuqp o" *xgewo " pq" 3:" n f|" 9; icfkgo+."wutcu"vt u"mk pkuclqu"r v lwoqu"uc   oc xkgpw"xck fkxcu"kpvtcxgpq|"cu"38 o ilmi"fgxcu0

Mqrwo "472"pq"542 rcekgpvkgo"uc   oc xkgpw"38 o ilmi"fgxcu"qdknvqmucmukocdc0"Ct rccwiuvkp vu" lwv dw"ucakuv v u"dncmwurct f dcu"*vqtuvatr k|ukvuvwokk+"acf s"; " *44"pq"472+"-q"r v o q"rgtuqpw."pq"mwr o" xkgp "icf lwo"kph |klcu"ncak kguv l u"cpahknml"rccwiuvkp vcu"lwv dcu xck"cpahknmcugu"f   kph |klw r tvtcwec"5 ' "*:"pq"472+"rcekgpvw0"

Xkudkgfl m"|k   qv u"dncmwurct f dcu"dkkc"icnxcuu rgu"*6; r v o o"rgtuqp o"pq"472+."kkg|g"*6 ' ." ; r v o o"rgtuqp o"pq"472+"wp"p vtgpg"*4 ' ."8 r v o o"rgtuqp o"pq"472+0

Xkudkgfl m"pqx rqv u"dncmwurct f dcu"rkto vt u"uvwpfw"ncik "r e"kph |klcu"u mwo c"dklc"pkg|g"*p:0" 4.: ' +."n vtgpg"*p = 8."4.6 ' +."icnxcuu rgu"*p = 6.13 8 ' ."k|uvwo k"*p = 5."3.4 ' +."mngrwu"*p = 5." 3.4 ' +."tgkdqpku"*p = 5."3.4 ' +"*kgumckvqv"tgkdqpk"wp"icnvcu itkg-cp u"ucj w+0 V Rktomj u"vt u"uvwd u"r e"kph |klcu"tcf s"- fcu"uo o ci cm wurct f dcu"|p vtgpg"*p = 3."2.6 ' ."kkg|g *p = 3."2.6 +"wp"o owiwtcu u"rgu"*p = 3."2.6 ' +0 Xkudkgfl m"pqx rqv "dncmwurct f dc"5"n f|"46 uvwpfw"ncik "r e"kph |klcu"u mwo c"dklc"icnxcuu rgu"*p?5." 3.4 ' +0

Pgx nc o q"dncmwurct f dw"uctcmcvu"vcdwncu"xgkf

60 vcdwn "kt"pqt f vcu"ct"qdknvqmucmukocdc"nkgvq-cpu"ucksu v u"pqx rqv u"dncmwurct f dcu"472 xgugn o" r v ocj o"rgtuqp o."wutcu"uc   oc xkgptgk| lw."kpvtcxgpq|w"38 o ilmi"qdknvqmucmukocdc"fgxw."ncu"kr" ucm tpqvcu"vcdknuq-k"qri pw"ukuv o"mncukhkm eklck"wp"vq tc-cp u"dkgflwoo m0

Dncmwurct f dw"dkgflwou"kt"fghkp vu"- fk<" qtv"dkgflk"*× 3132+."dkgflk"*pq"× 31322"n f| < 3132+"wp tgv m"*pq" × 313 222"n f| < 31322+0"Mcvt "ucsvqro dcu"dkgflwoc"itwr "pgx nc o u"dncmwurct f dcu"kr pqt f vcu"vq uoaciwoc"rcm rgu"ucoc|kp lwoc"uegg d 0

4. vcdwnc0"\k   qv u"dncmwurct f dcu"xgugnkgo o "rkgcwiw-clgo

MedDRA qti pw"ukuv o w" mncukhkm eklc	Dkgflk"	Tgv m
Ko p u"ukuv ocu"vtacw lwok		Cpahknmvkukc"tgcmeklc"
		Rccwiukp vc"lwv dc

6

MedDRA qti pw"ukuv m" mncukhkm eklc	Dkgflk"	Tgv m
Pgtxw"ukuv ocu"vtcwe lwok	Icnxcuu rgu	Tgkdqpku Rquvwt nu"tgkdqpku Jkrqguv |klc
Cew"dql lwok		Hqvqhqdklc
Cwuu"wp"ncdktkpvc"dql lwok		Pgrcv mcoucsl vc"cwu
Cukpuxcfw"ukuv ocu"vtcwe lwok		Hngd vu
Gnrq-cpcu"ukuv ocu"vtcwe lwok." mt –mwtxlc"wp xkfgpgu"unko dcu	Mngrwu	T mngu"mcktkp lwou" Fkuhqpklc" U pwuu"pqurtquvqlwok" Ck|fwuc
Mw c-|ctpw"vtcmvc"vtcwe lwok		U rgu"n r u
fcu"wp"|gm fcu"cwuf"dql lwok	Pkg|g."p vtgpg. k|ukvwok	Cngt kumcu"fgom ey vu" Xkur t lk"k|ukvwok" fcu"nqd cp u
Umgngvc-mwumw w"wp uckuvcwfw"ukuv ocu"dql lwok		U rgu"gmuvtgm kv v u" Owumw w"urc|ocu" Owumw w"tcwuv –cp u" U rgu"flqmn
Xkur t lk"vtcwe lwok"wp tgcmeklcu"kgxcf –cpcu"xkgv	U rgu"kph |klcu"xkgv	U rgu" Fkumqhqtvcu"ct mt –mwtx " Ftgdw k" Pqiwtwou" Rkgv mwou"kph |klcu"xkgv " Pgmctfk ncu"u rgu"mt –mwtx " Lwv iwou" U rgu"cukpuxcfc"rwpmeklcu"xkgv

Cvugxk– w"pgx ncmq"dncmwuract f dw"crtcmcuvv

Rccwiuvkp vc"lwv dc"wp"cpchkncmug

Dncmwuract f dcu."rct"mwr m"|k qvu": r mcl m"rgtuqp m."mc"kgur lcm u"rccwiuvkp v u"lwv dcu"f vkmc" r tvtcmvc qdknvqmucmukmocdc"kph |klc." dklc"p vtgpg. k|ukvwok." mngrwu." pkg|g. tgkdqpku. t mngu"mcktkp lwou."fkuhqpklc."gnrcu"vt mwu"wp"fkumqhqtvcu mtc –mwtx r l m"r v m m"rgtuqp m"mct"rccwiuvkp vw"lwv dw icnxgpqm mt"dklc ct" fw"uccuv vk"ukmq rvqok."rkgm tcm."kg|g"wp"k|ukvwok."wp"8 p v m u"rgtuqpcu |k olc"rct mngrw0 Cpchkncmugu "nckm " icpfr |"w"xkuc gtmg c."vquvctp mcmnc. mt –mwtxlc." mwiuvcu."x fgtc."tqm w" lc"m l m."dklc"fkh |."pkg|q–k"p vtgpgu"vkrc"k|ukvwok."gnrcu"vt mwu"wp"mngrwu0

Pgvkmc i vk"rkgt f lwok"rct vq." mc"ekvqm pw k|fcl –cp u k|itcmm"rccwiuvkp vcu"lwv dcu tgcmeklcu"wp" k|ukvwowu0 Nq| icu"k|lc"k|mvqm pqu"pgvkmc"pqx rqtvcu0

Im ngmit

Vt u"mnk pkkpqu"r vlwuqu"xkukgm "rcekgpvgm ."mwtk uc mc"xkgpvgtkg| lwu"wp"fwdwnvv"qdknvqmucmukmocdc"fgxw." pqx tv lc"qdknvqmucmukmocdc"cpvkxkgnw"xgkfq–cpqu0"Cuvq mr v m m"rgtuqp m"*4.7*:1542++."mcu uc qc"xkucm|"xkgpw"kpvtcxgpq|w"qdknvqmucmukmocdc fgxw."dklc"pq|kv xc rtu –cpcu"tcf vq"vgtcrgkvkumq cpvkxkgnw"*treatment-emergent anti-vjgtcrgwvke" cpvkdqf{ — ATA+"cvdknfgu"tgcmeklc0 Mxcpvkvcv xkg"vkvtk dklc"|gm — tqdgfl u"pq"3‹42"n f|"3‹5420"Pgdklc"rgt f lwou"rct"hctmcmqmkp vkcu"xkc"vqmukec vgu"rtqhknc k|ock m m"rcekgpvkgm ATA cvdknfgu"tgcmeklw0

\k q-cpc"rct"kgur lcm m"pgx ncm m"dncmwuract f d m

Kt"uxct ik"|k qv"rct"kgur lcm m"pgx ncm m"dncmwuract f d m"r e"| w"tg kuvt eklcu0"V f l fk"| w kgiwxwocltkumc"cvvkgec dc"vkgm"pgr tvtcwvk"w|tcwf| vc0"Xgugl dcu"cpt rgu"urgek nkuvk"vkgm l   iuk"|k qv"rct lgdm f m"kgur lcm m"pgx ncm m"dncmwuract f d m."k|ocpvqjq"X rkgnkmw m mkp vq"pcekqn u" |k q-cpcu"ukuv ocu"mqpcvkphqto eklw0

4.9. R tfq| -cpc

R tfq| -cpcu"icf lwo "rcekgrv|l pqx tq."ncl"pqvgkmvw."xck"pgtqfcu"lgdm fcu"pgncdx n icu kgvgm o gu"
rc| o gu0

70   HCT O CMQNQ KUM U" RC™ DCU

703.   Hct o cmqfkpc okum u" rc- dcu

Hct o cmqvgtcrgkvkum "itwrc‹ko   pugtwok"wp"ko pinqdwn pk."urgekhgumb pinqdwn pk."CV "mqfu‹
L28DD44

Fctd dcu"o gj pkuo u

Qdknvqmucmuk o cdu"kt"o qpqmnqp nc"cpvkvxkgnc."mcu"uckuv u"ct"*B. anthracis* ck|uct'i lq–q"cpvki pw"*CC+0"
Qdknvqmucmuk o cdu"pqo e"CC"uckuv –cpqu"ct"v "– pw"tgegrvqtkgo."pqx t-qv"Ukd tklcu"o tc"ngv l "hcmvqtc"
wp"v umcu"hcmvqtc."mcu"kt"vqmu nc"gp| o w"ucuv xfc   cu."mwtcu"k|tckuc"Ukd tklcu"o tc"vqmu nc"rcvqg pq"
kgfctd dw."kgm   –cpw"- p u0

Hct o cmqfkpc okum "kgfctd dc

Qdknvqmucmuk o cdu"uckuvc"dt xq"CC"ct"chfkpkv gu"uvcekqp t u"h |gu"fkuqek eklcu"mqpuvcpvk"*Mf+"2.55 pO0"
In vitro qdknvqmucmuk o cdu"rkguckuv u"*B. anthracis Ames.*"*Vollum* wp "*Sterne* egno w"CC0"CC"gkvkqru."ct"
mwtu"qdknvqmucmuk o cdu"uckuv u."vkgm"uc incd vu"|k   qvc *B. anthracis* egno mu0

™ pw"*in vitro* r v lwoki"ct"rg   w"o cmtqh ikgo "nkgekpc."ac"qdknvqmucmuk o cdu"pgk|t"ngv l "vqmu nc"
*CC +"ngv l "hcmvqtc mq o dkn eklc"vqmukumq"kgvgm o k0"

In vivo ghgmvkvkv gu"r v lwoqu"ct"Lcwp| ncpfgu"dcnvklkg "vtw–kgo "wp "*e{pqo qn iwu"o cec swgu.* mq"kpjke lc"
ct"*B. anthracis Aimes* egnom c"urqt o"kpjcn eklcu"eg   ."r c" tuv –cpcu"ct"qdknvqmucmuk o cdw"vkmc"
mqpuvcv u"tq pq"fgxcu"cvmct ig"k|k |f xqv dcu"t f v lc"rcnkgnkp lwou0"R c"ucumctcgu"ct"*B. anthracis* urqt o "
CC"mqpegpvt eklc"Lcwp| ncpfgu"dcnv"tw-w"wp "*e{pqo qn iwu"o cec swgu* ugtww " rcnkgnkp l u0"R c"
  tuv –cpcu"ct"qdknvqmucmuk o cdw"xckvwo o k|k |f xqlw–q"f xpkgmw"CC"mqpegpvt eklc"uc o c k|k |f l u0"CC"
mqpegpvt eklc"rncegdq "itwrcu"f| xpkgmkgo "rcnkgnkp l u."n f| "vkg"pqo ktc0

Ghgmvkvkv vg"

V "m "mqpvtqn wvu" mn pkumqu"r v lwowu"eknx mkgo "ct"kpjcn eklcu"eg   "kgi   vw"Ukd tklcu"o tk"pcv"kgur lc o u"
xgkmv"xck"vcu"pcx" vkumk."qdknvqmucmuk o cdc"kgfctd iwou."nkgvkjlqv"vq "o qpqvgtcrkl "ucn f|kn lwo "ct "
rncegdq"kpjcn eklcu   "kgi vc"Ukd tklcu"o tc" urt –cpc."kt"rc o cvqtvu"ct"ghgmvkvkv vg"r v lwokgo "ct"
Lcwp| ncpfgu"dcnvklkg "vtw-kgo "wp "*e{pqo qn iwu"o cec swgu0*

™clqu"r v lwo qu"f| xpkgmwu"kphke lc"ct"cvtwkvxgpk"422zNF_{72} cgtquqnxgkfc"*B. anthracis* urqt o "*Ames
egnom u+"wp "r c"vcm "vuv lc"ct"qdknvqmucmuk o cdw"fcfl fqu"nckmc "rwnkmqu0"Kpjcn eklc"eg   "kgi vc"Ukd tklcu"
o tc" urt –cpcu"r v lwo qu"f| xpkgmkgo "nkgvkvlc"| lgu"r c"vcm o."mcf"vkg m rct f l u"ukuv mumc"Ukd tklcu"
o tcmn pkum u"rc| o gu"xck"uk mrvmuok0"R ekgdctd dcu rtqhknmcmmgugu"r v lwo qu"f| xpkgmwu" tuv lc"r c"
B. anthracis kgfctd dcu."dgv"rktokus"uko rvm ow"rct f –cp u0"*E{pqo qn iwu"o cec swgu tus lc."mcf"
B. anthracis CC"tg|wnv vk"dkdlc rq| kv xk"ugtwm c"gnkgmvtkqhqtg"okmu"kpkuingmgugu"*ECL+"vgtu ."xkf lk"cpvkvxkgnu"
62 uvwpfcu"r c"rcm   cu-*B. anthracis* kgfctd dck0"Vgtcrgkvkumq"r v lwo qu"ct"Lcwp| ncpfgu"dcnvclkgo "
vtw-kgo "f| xpkgmk"vkmc "uts ut kt"r c"rq| kv vc"CC"*ECL* vguts tg|wnv vc"xck"cpg rgp tglq-cu" gtm c"
vgo rgtcv   tcu"rccwiuuk –cp u "xktm o qvp l u.xkf lk"cpvkvxkgnu"52 uvwpfcu"r c"kphke –cpcu0"K|f| xqv dw"
v n m"cptcmu vclqu"r v lwo u x tv lc"4: fikgpcu"r c"kphke –cpcu"ct"*B. anthracis0*

Xkgptgk| lcu"kpvtcxgpq|cu"qdknvqmucmuk o cdc fgxcu."mq"nkgvqlc k "o qpqvgtcrklw."ghgmvkvk tk"kpjcn eklcu"
eg   "kgi vc"Ukd tklcu"o tc" uts –cpk"pqx tv lcxkgp "r v lwo ct"Lcwp| ncpfgu"dcnvclkgo "vtw-kgo "wp"vt u"
r v lwo qu"ct"*e{pqo qn iwu"o cec swgu* *CR424."CR426"wp"CR523+"xkuk"r v lwoki"dklc"ct"rncegdq"

8

mqpvtqn vk."pglcw–kp vk"wp"cvdknuvq–k"NNR"rtcu d o0"R v lwok"CT255."CR424"wp"CR523"dklc" o cum vk."wp" r v lwou"CR426"dklc" o cum vu"itwrck0"

70 vcdwnc0"K|f| xqv dcu"t f v lk" o qpqvgtcrlcu"ghgmvkxkv gu"r v lwo qu"ct"qdknvqmucmuk o cdw" ***38 o i** l**m i** +

	K|f| xqv dcu"rtqrqteklc"r v lwo c"dgki u * ' "]k|f| xqlclp_+		r–x tv dc²	;7 ' "VK³
	Rncegdq	**Qd**knvqmucmuk o cdu" **38 o i**l**m i**"		
tuv –cpc — Lcwp| ncpfgu"dcnvkg"vtw–k				
R v lwou"CT255¹	2"*2135+	83.7 ' "*:135+	2.2235,	*2.4;2.'2.':83+
tuv –cpc — *Cynomolgus macaques*				
R v lwou"CR426¹	8 ' "*3138+	68.9 ' "*9137+	2.228:,	*2.2:;.'2.8:3+
R v lwou"CR424¹	2"*2139+	53.5 ' "*7138+	2.22:7,	*2.29;.'2.7:9+"
Rtqhkncug"r e"kgfctb dcu — *Cynomolgus macaques*				
R v lwou" AP301⁶	3:j r e" kgfctb dcu	2"*2l8+	100 % *8l8+	2.2234,	*2.693."3.222+
	46 j r e" kgfctb dcu	--	:5 ' "*7l8+	2.2264,	*2.452."2.;;8+
	58 j r e" kgfctb dcu	--	72 ' "*5l8+	2.2567	*-2.259."2.::4+

VK<"vkec o dcu"kpvgtx nu

[1] K\|f\| xqv dc"vkmc"x tv vc"4: fkgpcu"r e"kphke –cpcu"ct"urut o ="xkukg o "tcpfqmk| vclkg o "f\| xpkgkgk o." mc o "rktrou" tuv –cpcu"dklc"rq\|kv xu"dcnvgtk o ilcu"tg\|wnt vu=" tuv –cpcu"w\|u m–cpw"k\|tcku lc"pq\| o ic" gtr o e c"vgo rgtcv tcu"rccwiuvp –cp u"*r v lwou"CT255+"xck"rq\|kv xu"tg\|wnt vs"ci|ssct lq–q"cpvki pw" gngmvtqjgo knwokpkuegpegpcg"vguv *r v lwok"CR426"wp"CR424+0

[2] r–x tv dc"kgig vc"xkgprwu l "*Boschloo* vguv "*ct"*Berger-Boos* ico ocu" o qfhkhk e k|w = 2.223+" ucn f\|zp l wo "ct"rncegdq

[3] Rtge \|u";7 ' "vkec o dcu"kpvgtx nu"k\|f\| xqv dcu"t f v lw"uvctr cdk

[6] K\|f\| xqv dc"vkmc"pqx tv vc"4: fkgpcu"r e"kphke –cpcu"ct"urut o 0" ∉ Cr\| o "uvcvkuvkkmw"b vkumw o "2.247"n o gn

Rgfkcvtkum "rqrwn elc

Gktqrcu"\ w"c gpt tc"cvnkgp"rkgp mwow"kgupkeig t"r v lwo u"tg\|wnt vu"rct *NYXTHRA* kkgp "xck" xckt m u"rgfkcvtkum u"rqrwn elcu"cncm–itwr us"dcekn tcu"kphgmeklcu" tuv –cpck"*kphqto eklu"rct"nkgvkq–cpw" d tnkg o "smcv t"6040 ctcm–wpmt +0

™ s| o gu"ktr iuvt vcu"ök| o owc m tv ö0"Vcu"pq\| o ."mc"ucmcct "ct– u"unk o dcu"tgvww o "wp" kkmw" crvx twow"f "pcx"dklku"kgur lcu"kgi v"rikp iw"kphqto eklu"rct– o\|l n o0" Gktqrcu"\ w c gpt tc"kk"icfw"r tdcwfd"cwpkig vq"kphqto eklu"rct"- o\|l n o "wp"xclcz| dcu"icf lwo " cvlcwpkpc"-q\|| w"crtcmuvw0

7040 Hct o cmqmkp vkm u" rc– dcu

W\|u m–cp u

Qdknvqmucmuk o cdc"hct o cmqmkp vkmc"kt"nkpg tc"fgxw"fkctc|qp "pq"6 o i l m i "*2.47"tgk\|o c|k "kgvgkecoc" fgxc+"n f|"38 o i l m i"r e"xkgpt gk|lcu"kpvtcxgpq|cu"kgxcf –cpcu"xgugn o "r v o o "rgtuqp 0"R e" xkgpt gk|lcu"kpvtcxgpq|cu"38 o i l m i"qdknvqmucmuk o cdc"fgxcu"kgxcf –cpcu"xgugn o "x tkg–w"wp"ukgxkg–w"

9

f|kowoc"r v o o"rgtuqp o"xkf lcku"Eₒcz wp"CWEₖₚₕ cvvkgc ik"dklc"622 ± ;3.4 omilon"wp"
7392 ± 3582 omi"fkgp lon0"Qdknvqmucmukocdc"gnkomn eklcu"rwurgtqqu"dklc"cvvwxgpk"42 fkgpcu"*xkf lk+0

<u>K|mnkgfg</u>

Xkf lcku"qdknvqmucmukocdc"k|mnkgfgu"vknrwou"n f|uxctc oqpcegpvt eklcu"cru m qu"dklc"9;3;±4 onlmi"
wp"nkgl mu"pgm "rnc|ocu"vknrwou."mcu nkgekpc"rct"k|mnkgfk"cwfqu0

<u>Dkqvtcpuhqto eklc</u>

Ct"qdknvqmucmukocdw"pcv"xgkmvk"qhkek nk" gvcdqnkuoc"r v lwok0
Vqo"r oqpqmqp nq"cpvkxkgnw"k|xkgvqlwou"rctcuvk"kgvxgt k|mnkgfk" trwu"cukpuxcfw"vgnrcu."kgur lcou."
w|u eqvkgu"cwfqu."wp"rtqvg flw"mcvcdqnkuou"n f|"ocz|gio"rgp fkgo"wp c okpqumo d o."mcu p c"e"vcvo"vkgm"
kgm cwvcu"gpfqincpq "mqp "xck"k|xcf vcu0

<u>Gnkomp eklc</u>

Xkf l u"qdknvqmucmukocdc"mn tgpuc"x tv dcu"dklc"5.57 ± 2.;54 onlfkgp lmi"wp"fcwf|"ocz| mcu"pgm "
inqogtwnw"hknvt eklcu" vtwou."mcu nkgekpc"rct"vq."mc"qdknvqmucmukocdc"mn tgpuu"ecwt"pkgt o"icpfd |"pcx"
pqvkeku0

<u> rc-cu"rqrwn eklcu</u>

F|kowoc."xgewoc"wp"tcugu"kgvgmog
Qdknvqmucmukocdc"hctomqmqkp vkmw"x tv lc."xgkeqv"rqrwn eklcu"hctomqmqkp vkcu"cpcl |k."k."k| ocpvqlqv"
ugtwoc"rctcwiwu"pq 592 xgueg o"r v ocl o"rgtuqp o."mwtcu"6 mn pkumiu"r v lwoqu"uc oc"xkgpw"
kpvtcxgpq|w"fgdw0"Rc ocvqvkgu"w|"-q"cpcl |k."f|kowoc"*ukgxkgv o "ucn f|kp lwo ct"x tkg-kgo+."tcugk"
*ekvw"tcruu"r tv xlkgo"ucn f|kp lwo ct"dcnv u"tcugu"r tv xlkgo+"xck"xgewoco"*icfqu"xge mkgo "
eknx mkgo"ucn f|kp lwo ct"lcwtkgo"eknx mkgo+"dklc"pq| o icu"kgvgmogu"w|"qdknvqmucmukocdc"
hctomqmqkp vkumcklgo"rctcogvtkgo0"Vc w"qdknvqmucmukocdc"mn pkumclqu"r v lwou"pgdklc"kgm cwvu"
rkgvkgmco u"umckvu"r v oq"rgtuqpw."mcu dklc 87 icfwu"xgecu xck"xge mcu."nck"pqvgkmvw."xck"vq"
hctomqmqkp vkmc"cv- ktcu"pq"lcwp mw"r vo"rgtuqpw"hctomqmqkp vkcu0"Pq"542 r v ocl o"rgtuqp o."
mcu"vkc"kgm vcc"qdknvqmucmukocdc"mn pkumclqu"r v lwou.";.6 ' *521542+"dklc"87 icfwu"xgecu"wp"
xge mcu."dgv"4 ' *81542+"dklc"97 icfwu"xgecu"wp xge mcu0

Ct" gtog c"k/o tw"ucuv vc"kgvgmog
Mn tgpuu"rkg"nkgncu gtog c"ocucu"*32; mi+"dklc"crvwxgpk"rct"5: ' "nkgl mu"pgm "cvucwegu"rqrwn ekl 0"V "
tg|wnt v "r e"ocuck rkgl iqvcu"fgxcu"nkgvq-cpcu"*38 oilmi+"CWEₖₚₕ rcnkgplp l u"rct"34 ' ."mcu"pcx"
mn pkumk"pq| o iu"rkgecwiwou0

Rgfkcvtkum "rqrwn eklc
Qdknvqmucmukocdc"hctomqmqkp vkc"d tpkgo"pcv"pqx tv vc0"Kgvgmkwok"rct"fgx o."mcu"okp vk"40 vcdwn "
*6040 crcm-rwpmvu+"kt ige vk"ukoun eklu."k|z ocpvqlqv"rqrwn eklcu"HM"rkgglw."mcu"k|uvt f vc."nck"cvdknuvw"
pqx tqvclck"qdknvqmucmukocdc"kgfctd dck"rkgecwiw-cklgo."nkgvqlqv38 oilmi"fgxw0

7.5. Rtgmn pkumclg"fcvk"rct"ftq-wow

Pgmn pkumclqu"uvcpfctv v lwou"kgi vkg"fcvk"rct"hctomqnq uiuq"ftq-wow."cvm tqvwt"fgxw"vqmukekv vk."
vqmukkumw"kgvgmok"w|"tgrtqfwmvkxkv vk"wp"cvv uv dw"pgnkgekpc"rct" rc-w"tkumw"eknx mco0

Egpvt n u"pgtxwukuv oc"*EPU+"dql lwok"*dcat tklcu."kgcckwoou."uck q-cpc"wp"fcflm tv"pgmtq|g+"vkc"
mqpuvcv vk"ct"Ukd tklcu"o tk"kphkc vclqu"pgk|f xqlw-clqu"Lcwp| ncpfgu"dcnvcdcu"tvw-qu"wp"*e{pqoqniwu*
ocecswgu."mc kpvtcxgp|k"kgxcf lc"qdknvqmucmukocdw"*×6 oilmi+."xck"mqpvtqngu"nckm ."cf"vkc"
cruvkrtkp tc"tcucnkocpc0"Okmtqumqrkumca"r ock cu"pgk|f| xqlw-clqu"f| xpkgmqu."mwtk uc oc"
qdknvqmucmukocdw."dklc"cukuvcu"ct gmuvcxcmnwn tw"dcaj tklw"mn vd vk."gpxkui"qdknvqmucmukocdc"kgvgmok0
Icnxcu"uocf|gu"w"jkuvqrcvqnq kl "pgkik"mqpuvcv vcvcvdknfgu"tgcmeklcu"cvtcr dc"pq"fgxcu0"Ct" tuv -cpw"
uckuvc vtu"uocf|g "w"dql lwouu"pgmqpuvcv lc"ct"Ukd tklcu"o tk"kphkkc vclim."k|z| xqlw-clgo "Lcwp| ncpfgu"

dcnvclkg o"vtw–kg o"*4:0 fkgp +"xck"*e{pq o q∩iwu" o cecswgu *∩ f|"780 fkgpcik+"cvvkeg ik"r e"xkgptgk| lcu" qdknvqmucmuk o cdc"fgxcu"∩ f|"38 o ilmk"wp"∩ f|"54 o ilmk"nkgvq–cpcu0"R e" tuv –cpcu"ct"qdknvqmucmuk o cdw" ct"Ukd tklcu" o ik"kpnhke vclkg o."k|f| xqlw–clkg o"*e{pq o q∩iwu" o cecswgu pgvkmc"pqx tqvk"ct" qdknvqmucmuk o cdw"uckuv it"pgktqdkjgkxkqt nk"ghgmvk0

Xkgpu"g o dtklw"wp"cwi w"cvv uv dcu"r v lwo u"vkmc"xgkmvu"it upkgo."xgugnkg o"Lcwp| ncpfgu"dcnvclkg o" vtw–kg o."mwtk iguv eklcu"80."320."350"wp"390 fkgp "uc   o c"6"kpvcxgpq|cu"qdknvqmucmuk o cdc"fgxcu."mcu" ucupkgf|c"54 o ilmk"*4 tgk|gu"nkgl mc"fgxc"rct"eknx mc"nkgvqvq|q"fgxu."k|ucqv"m   o ilmk+0"Pgvkmc"igk vk" rkgt f lwok"rct"mckv lwow"it up o"o vv o "xck"cwiik o "qdknvqmucmuk o cdc"nkgvq–cpcu"f   0"Mwowncv x " kgfctd dc"w|"Lcwp| ncpfgu"dcnvclkg o"vtw–kg o"*32 222"o miÉfkgp 1on+"rkg"pgpqx tqjc o u"pgncdv n i u" kgvgkm o gu"n o g c *NOEL+ 54 o ilmk1fgx *p = 6"fgxcu+."rc o cvqvqvkgu"w|"CWE₀₋₃₇ fkgp o."dklc"cvwxgpk" fkxcu"tgk|gu"nkgl mc"rct"v xk u"wp"o v –w"crxkgpqvq"xkf lq"CWE."nkgvqlqv"38 o ilmk"∩n pkusq"kpvtcxgpq|q" fgxw0"E₀cz x tv dcu"r e"54 o ilmk"fgxcu"nkgvq–cpcu"dklc"33:0 o eiÉfkgp 1on0

Mcpgtqigpv vgu."igpqvqmukekv vgu"wp"hgtvknkv vgu"r v lwok"ct"qdknvqmucmuk o cdw"pcv"xgkmvi0

8. HCTOCEGKVKUM "KPHQTO EKLC

8.3.   Rcn ixkgnw"uctcmuvu

 Jkuvkf pu
Uqtd vu"*G642+
Rqnkuqtd vu":2"*G655+
U nuum dg"*G729."r J"n o g   c"rkgn iq–cpck+
P vtklc"jkftqmu fu"*G746."r J"n o g   c"rkgn iq–cpck+
    fgpu"kplgmeki o

8.4.   Pgucfgt dc

™ u"| ngu"pgfed muu"ucicwv"*nkgvqv"o cku lw o +"ct"ekv o| n o."k| goqv"8080 crcm–rwpmv "o kp v u0

8.5.   W|incd –cpcu"nckmu

 Pgcvx tvu"hncmqpu

9 icfk

 Cv– ckf vu–   fwo u"kph |klcu" o cku

R e"cv– ckf –cpcu"kph |klcu" o cku "   okmk ."hk|km n "wp" o kkqtdkqnq kum "uvcdknknkgvq–cpcu"nckm kt" rkgt f vc":uuwpfcu"kuvcdcu"vg o rgtcv t "*42 °C–47 ÅE+"xck"ngfwuucr "*4 °C–: ÅE+0

Pq" o kmtqdkqnq kum "xkgfqm   c"–u" ngu"kt"k k|kgvq"pgcvx lqvkgu."lc"xkggp"c–cpcu 1ucicvxq–cpcu 1" cv– ckf –cpcu o gvqfg"pgk|un f|" o kmtqdkqnq kum "rkgu   qlwo c"tkumw0

Lc"v u"pgvkgkm"k|kgvqvcu pgmcx lqvkgu."rct"w|incd –cpcu"nckmw"wp"w|incd –cpcu"crv kgo cvbknf iu"kt" nkgvq lu0

 Cv– ckf vu–   fwo u–ktc "kph |kl o "

Mcf"kt"ucicvxq–cpcu"cv– ckf vu"NYXTHRACIS – fwo u."vcu"l k|kgvq"pgcvx lqvkgu."pgxku"l w|incd 0" Pgk|o cpvq u"| ngu"l k o gv0

8.6.   rc–k"w|incd –cpcu"pquce lwok

W|incd v"ngfwuucr "*4 °C–: ÅE+0

Pgucucnf v0
W|incd v"qtk kp ncl "kgrcmqlwo .''nck"rpcucti vw"pq"ickuocu0

W|incd –cpcu''pqucce lwowu''r e'| w''cv– ckf –cpcu''umcv v'8o5m-rwpmv 0

807.   Kgrcmqlwo c''xgkfu''wp''ucvwtu

822 oi!8 on''mqpegpvt vc''hncmqp "*K vkrc''ustknu+''ct'igwoklcu''ckjd |pk''wp''rqnkrtqprn pc''x ek w''ct"
cnwo pklc''crxcnmqlwow0
Kgrcmqlwo "kt'3 hncmqpu0

808.   rc–k''pqt f lwok''cvtkvtwuw''nkmxkf –cpck''wp''ekvk''pqt f lwok''rct''t mq–cpqu

<u>Uxct ik''pqt f lwok''rct''ucicvcxq–cpw</u>

¢   Mqpegpvt vs''kpnjgeckw– fwoc''rcicvcxq–cpck''rktou''nkgvto–cpcu''xk|w nk''I r tdcwfc.''nck''nqvgkmvw.''
    xck''vcl "pcx"fc   k w''xck''mt ucu''k|ock w0''*NYXTHRACIS*|kftu''n f|''qrenguegpvu.''dg|mt uckns''n f|''
    ick–k''f|gnvgpusjick–k''dr pcpck''f|gnvgpu– fwou.''mwu–''xct''ucvwt v''fcflcu''ecwtusr f icu''n f|''bcnvcu''
    rqvge pc''fc   k   cu"* mcu''vkmu''cefonpklu''hknvtc''rcn f| dw+0
¢   K| ogvkgv''hncmqpw.''lc– fwoc''mt uc''kt ockpjlwusjes''xck''vcu''ucvwt uxg–cu''fc   k cu"*umcv v'
    50 crcm-rwpmv+0
¢   Pgmtcvkgv''hncmqpw0

<u>Ucicvcxq–cpc''wp''cv– ckf –cpc''kph |klcu''ocku "</u>

30   Crt kpkgtc''xclcf| iqu qdknvqmucmkocdc''oknkitcowu.''tgk|kpqv''kgvgkecoq''o ilmi''fgxw''40 vcdwn "
     *umcv v'6o040 crcm-rwpmv+''ct''rcekgpvc gtoge c''o cusw''mknqitcomu0
40   Crt kpkgtc''fgxck''pgrikecke–coq''qdknvqmucmkocdc''mqpegpvt vc''kph |klw– fwoc''rcicvcxq–cpck''
     vknrwvu''oknknkvtqu''wp''hncmqpw''umckvw.''k|fcnqv''crt kp vq''fgxw''oknkitcomu''*30 fctd bc+''ct''
     mqpegpvt cklu''322 oilon0''Mcvt "hncmqp "kt'8 on''qdknvqmucmkocdc''mqpegpvt vc''kph |klw– fwoc''
     rcicvcxq–cpck0
50   K|x nkgvkgu''rkgo tqvc'k'o tc''kph |klcu''ocksuw.''co''oilon''*2.; '+''p vtkkc''jnqt fc– fwow''
     kpnjgeckl o 0''K|xcfkgvv fw– fwow''fcwf|wow''pq''kph |klcu''ocksuc.''mcu''xkgn fs''ct''40 fctd d "
     crt kp vq''qdknvqmucmkocdc''fcwf|wow''oknknkvtqu0''K| ogvkgv– fwow.''mcu''vkmc''k|xcf vs''pq''
     kph |klcu''ocksuc0
60   K|xcfkgv''xclcf| iq''qdknvqmucmkocdc''mqpegpvt vc''kph |klw– fwoc''rcicvcxq–cpck''fcwf|wow''
     *crt kp vs''40 fctd d +''pq''*NYXTHRACIS* hncmqpc*-kgo +0''K| ogvkgv''lgdk fw''pgik|nkgvqtq'| w''fc w.''
     mcu''cvnkmwsk''*NYXTHRACIS* hncmqp "*-qu+0
70   R tpguikgv''xclcf| iq''qdknvqmucmkocdc''mqpegpvt vc''kph |klw– fwoc''rcicvcxq–cpck''vknrwo|w''
     k|x n vq''kph |lcu''ocksuw0
80   Xkgik nk''crx tuskgv''kph |klcu''ocksuw.''nck''uclcmvw– fwow0''Pgmtcvkgv''hncmqpw0
90   Kph |lc''l kgxcfc''xckt m''pgm ";2 okp –w''nckl "ct vtwuw.''mcu''crtcmuvs 50 vcdwn "*umcv v'
     6o040 crcm-rwpmv+.''k| ocpvqlqv''2.44 oktqrpw n pkcus''hknvtw0''
:0   Ucicvcxqvcvu– fwou''kt''uvcdknu: uwpfcu.''lc''vq |incd "kuvcdcu''vgorgtcv t "42 ÅE''n f|''47 ÅE.''xck''
     : uvwpfcu.''lc''vq |incd "ngfwuumcr "4 ÅE''n f|''* ÅE''vgorgtcv t 0

<u>Ucicvcxq–cpc''wp''cv– ckf –cpc'– kte "kph |kl o</u>

30   Crt kpkgtc''xclcf| iqu qdknvqmucmkocdc''oknkitcowu.''tgk|kpqv''kgvgkecoq''o ilmi''fgxw''40 vcdwn "
     *umcv v'6o040 crcm-rwpmv+''ct''rcekgpvc mcsu kknqitcomu0
40   Crt kpkgtc''fgxck''pgrikgcke–coq''qdknvqmucmkocdc''mqpegpvt vc''kph |klw– fwoc''rcicvcxq–cpck''
     vknrwvu''oknknkvtqu''wp''hncmqpw''umckvw.''k|fcnqv''crt kp vq''fgxw''oknkitcomu''*30 fctd bc+''ct''
     mqpegpvt cklu''322 oilon0''Mcvt "hncmqp "kt'8 on''*NYXTHRACIS* mqpegpvt vc''kph |klw– fwoc''
     rcicvcxq–cpck0
50   K|x nkgvkgu''– ktck.''mwtcu''k|o ts''kt''rkgo tqvu''mqp lcm''kgxcf o u''kph |klcu''vknrwocm0

6️⃣ K|ocpvqlqv"k|x n vq"– ktek"up"2o44tqpw"l piklcs"hknvtw."kgxgnekgv"xclcf| iq"qdknvqmucmukocdc" mqpegpvt vc"kph |klw"– fwoc"rcicvcxq–cpck"fcwf|wow"*crt kp vu"40 fctd d +0"K|ogvkgv"lgdm fw" pgk|nkgvqvq"| w"fc w."mddl/XxMXriiXHRACIS hncmqp *-qu+0"

7️⃣ Nck"rcicvcxqvw"40 vcdwn "pqt f vq"mqr lq"kph |klcs"crlqow."kgxgnekgv"cvdknuvq–w; o il on"*2.;'+" p vtklc"jnqr fc– fwoc"kplgmekl o"fcwf|wow0

8️⃣ W|ocp ik"uclcwekgv"– fwow0"Pgmtcvkgv0

9️⃣ R e"qdknvqmucmukocdc"cv– ckf v "– fwoc"rcicvcxq–cpcu"vq"pgmcv lqvkgs"kgxcfkgv0"Pgw|incd lkgv" – fwow"– kte 0"Pgk|nkgvqv s"| ngu"k|ogvkgv0

<u>Cvmtkvwow"nkmxkf –cpc</u>

Pgk|nkgvqv s"| ngu"xck"k|nkgvqvkgv"ocvgtk nk"l k|p ekpc"cvdknuvq–k"xkgv l o "rtcs d o0

7.   TG KUVT EKLCU"CRNKGE DCU" RC™PKGMU

UHN"Rjctocegwvkecnu"Fgwvuejncpf" I od J
 Octkg-Ewtkg-Uvtcuug":
9;75 "N¾ttcej
X eklc

8.   TG KUVT EKLCU"CRNKGE DCU"PWOWTU*-I)

GW13l42l36:7l223

9.   RKTO U"TG KUVT EKLCUlR TTG KUVT EKLCU"FCVWOU

Rkto u"tg kuvt eklcu"fcvwou‹"42420"icfc"3:0"pqxgodtku

10.   VGMUVC"P F L U"P TUMCV™CPCU"FCVWOU

U m mc"kphqto eklc"rct– o"| n o"kt"rkgglcoc"Gktqrcu"\ w"c gpv tcu"v ogm c"xkgvp ‹" <u>jvvr‹ll y y y0gmoc0gwtqrc0gw</u>"wp"}Fon dxcnuvu"C gpv tcu"pqucwmqus"*uckvg+¡"v ogm grpxk@0

II PIELIKUMS

C0 DKQNQ KUMK"CMV X U"XKGNCU"TCfiQV LU"WP"
    TCfiQV LU."MCU"CVDKNF"RCT"U TKLCU"K\NCKFK

B. K\UPKG I™CPCU"M TV DCU"WP"NKGVQ™CPCU"
    PQUCE LWOK"XCK"KGTQDGfiQLWOK

E0 EKVK"TG KUVT EKLCU"PQUCE LWOK"WP"RTCU DCU

D. PQUCE LWOK"XCK"KGTQDGfiQLWOK"CVVKGE D "W\"
    FTQ™W"WP"GHGMV XW"\   W"NKGVQ™CPW

E.   RC™CU"UCKUV DCU."NCK"XGKMVW"R ETG KUVT EKLCU"
    RCU MWOWU"\ N O."MCU"TG KUVT VCU"šK\   OWOC"
    M TV ö

A0   DKQNQ KUMK"CMV X U*-Q+"XKGNCU*-W+"TCfiQV LU*-K+"WP"TCfiQV LU*-K+."MCU"
CVDKNF"RCT"U   TKLCU"K\NCKFK"

Dkqnq kumk"cmv x u*-q+"xkgncu*-w+"tcflqv lc*-w+"pqucwmwou"wp"cftgug

Nqp|c"Dkqnqikeu."Kpe0"
323"Kpvgtpcvkqpcn"Ftkxg
Rqtvuoqwvj."PJ"25:23"
CUX

Tcflqv lc*-w+."mcu"cvdknf"rct"u tklcu"k|nckfk."pqucwmwou"wp"cftgug

CegtvkRjctoc"D0X0
Dquejuvtccv"73
6:33" IE."Dtgfc
P fgtncpfg

B.   K\UPKGI™CPCU"M TV DCU"WP"NKGVQ™CPCU"PQUCE LWOK"XCK"GTQDGfiQLWOK"

Tgegr-w"| ngu0

E0   EKVK"TG KUVT EKLCU"PQUCE LWOK"WP"RTCU DCU

¢ **Rgtkqfkumk"cvlcwpqlc o cku"ftq-woc"|k   qlwou"*RUWT+**

™q"| w"rgtkqfkumk"cvlcwpqlcoq"ftq-woc" qlwow"kgupkgi-cpcu"rtcu bcu"kt"pqr f vcu"Gktqrcu"
Ucxkgp bcu"cvucwegu"fcvwou"wp"rgtkqfkumq"|k qlwow"kgupkgi-cpcu"bkgflwoc"uctcmu "*EURD
uctcmu +."mcu"uciccvqvuucmc   "ct"Fktgnv xcu"42231:5lGM"3290kpvc"90 rwpmvw."wp"xkuku"
vwtrp mclqu"uctcmuvc"cvlcwpkp lwoqu."mcu"rwdnkkvk"Gktqrcu"| w"c gpv tcu"v ogm   c"xkgvp 0

D.   PQUCE LWOK"XCK"KGTQDGfiQLWOK"CVVKGE D "W \"FTQ™W"WP"GHGMV XW"\   W"
NKGVQ™CPW""

¢ **Tkumc"r txcnf dcu"rn pu"*TRR+**

Tg kuvt eklcu"crnkec bcu"pc-pkgmco"| vgke"pgrkeckg-co u"fctmcmqxkikncpegu"fctd dcu"wp"
rcu mwok."mcu"u m m"crtcmuv kt"tg kuvt eklcu"rkgvkmwoc"30:040 ofwn "kgm cwwcl "crvkrtkp vcl "
TRR wp"xkuku"vwtrm mclqu"cvlcwpcvlqu"crvkrtkp vclqu"TRR0

Cvlcwpkp vu"TRR"l kgupkgf|<
  ¢ r e"Gktqrcu"\   w"c gpv   tcu"rkgrtcu lwoc=
  ¢ lc"kgxkgusv itq| lwoktkumc"r txcnf dcu"ukuv m."lq rc-k"icf lwou."mcf"uc gomc"cwpc"
      kphqto eklc."mcu"xcr d vkumk"kgvgem t"kgiwxuwoltkumc"rtqhknw."xkck"pq| m iw"*fctmcmqxkikncpegu"
      xck"tkumc"oc|kp -cpcu+tg|wnv vw"ucupkgi-cpcu"icf lwo 0

E.   RC™CU"UCKUV DCU."NCK"XGKMVW"R ETG KUVT EKLCU"RCU MWOWU"\ N O."
MCU"TG KUVT VCU"šK\ OWOC"M TV ö"

V "m"- kt"tg kuvt eklc"õk| owoc"m tv ö"wp"ucuc   "ct"GM"Tgiwncu"Pt0 948|4226"360 rcpvc":0 rwpmvw."
TC "pqvgkmvcl   "nckmc"rqu o"| xgke"- fk"rcu mwok<

Crtcmuvu	K|rknfgu"vgt o k –
Nck"cruvkrtkp vw"qdknvqmucmuk o cdc"hct o cmqmkp vkmcu" o gvqfk"* I EN-382+"eknx mc"ugtwo ."tg kuvt eklcu"crnkge dcu" rc–pkgmc o "l kgupkgf|" vguvc"xcnkf eklcu"tg|wnv vk"cvvkge d "w|"v n m"pqt f vclkgo "curgmvkgo ." rktou"k| o cpvqv"vguvw"rctcwiw"cpcn|gk"mn pkumcl " r v lwo "CJ723‹" RC"*85"wp" : 5+."GH."NH"wp"CFC"kpvgthgtgpeg."m "ct "vguvc"xgkmvkvs lc" jg o qn vkumcl "wp"nkr okumcl "ugtwo 0"Rctcn nkuocl xgke"ct" rctcwikgo ."mcu"kgi vk"rn pqv "cvmn v "ncwmc"r v lwo "CJ7230	L kgupkgf|"mqr "ct"r v lwo c" CJ723"icl iq"mn pkumq" |k qlwow
Nck"pqx tv vw"mn pkumq"cvbknfgu"tgcmeklw."ftq–wow"wp"rcpguco dw." vquvctr"umk o bcu"icklw"wp"k|df| xqv bcu"t d v lwu"r v o o "rgtuqp m" ct"ckk|fqm o "rct"kpjcn eklcu"eg "kgi vw"Ukb tklcu"m tk"xck" kgur lcmw"xck"crurkrtkp vw"kpjcn eklcu"eg "kgi vw"Ukb tklcu"m tk."mcu"icku"|k qlwou"vkmu" tuv vcu"ct"qdknvqmucmuk o cdw."ucamc ct"crurkrtkp vq"rtqvqmqnw" tg kuvt eklcu"crnkge dcu" rc–pkgmc o "l xgke"r v lwo u"wp"l kgupkgf|" icl i "|k qlwo c"tg|wnv vk"ct"60 h |gu"cvmn vw"ncwmc"r v lwo w"CJ723" r e"Ukb tklcu" tc"w|nkgu o qlwo c"xcnuv u."mwt u"qdknvqmucmuk o cdw"kt" tg kuvt vu"wp"rkgglc o u0	Kgupkgf|co kg"icfc" |k qlwok"
	k\icl icku"|k qlwou"vkmu" kgupkgivu"pg"x n m"m " 34" o pg–wu"r e"r f l u " qdknvqmucmuk o cdc" kgxcf –cpcu"xck"r f lq"fcvw" crmqrq–cpcu"tgvtqurgmv x u" fcvw"x m–cpcu"icf lwo

III PIELIKUMS ●

OCT   LWOC"VGMUVU"WP"NƘGVQ™CPCU"KPUVTWMEKLC

C0 OCT LWOC"VGMUVU

ꞮPHQTO EKLC."MCU"L PQT FC"W\" T L "ꞮGRCMQLWOC

MCTVQPC"MCUV VG

---

1. \ W"PQUCWMWOU

NYXTHRACIS 100 o i l o n"uvgtknu"mqpegpvt vu
qdknvqzczk o cd"

---

2. CMV X U*-Q+"XꞮGNCU*-W+"PQUCWMWOU*-K+"WP"FCWF\WOU*-I)

1 o n‹"322 o i"qdknvqmucmuk o cdc

---

3. RCN I XꞮGNW"UCTCMUVU

Rcn ixkgncu‹"jkuvkf pu."uqtd vu."G655."u nuum dg."p vtklc"jkftqmu fu."fgpu"kplgmekj o0

---

4. \ HꞮQTOC"WP"UCVWTU

Mqpegpvt vu"kph | klw"– fwoc"rcicvcvxq-cpck
822 o il8 o n
1 hncmqpu

7⃝ NꞮGVQ™CPCU"WP"ꞮGXCF ™CPCU"XGꞮFU*-I)

Rkt o u"nkgvq-cpcu"k|ncukgv"nkgvq-cpcu"kpuvtwmeklw0 k0x0 r e"cv– ckf –cpcu0
Vkmck"xkgptgk| lck"nkgvq-cpck0
Pgmtcvkgv0

L kgm cwl"SꞮT"mqfu -"y y y0qdknvqzczk o cd-uhn0gw

8⃝ RC™ꞮK"DT FKꞮ LWOꞮ"RCT"\ W"W\ I NCD ™CPW"D TPꞮGO"PGTGF\CO "WP" PGRꞮGGLCO "XKGV

---

7. EKVꞮ" RC™ꞮK" DT FKP LWOꞮ."LC"PGRꞮGEꞮG™COU

---

8. FGT I WOC"VGTOꞮK ™

Fgt iu"n f|

---

9. RC™ꞮK"W\ I NCD ™CPCU"PQUCE LWOꞮ

W|incd v"ngfwuumcr 0"
Pgucucnf v0"

19

W|incd v"qtk kp ncl "kgrcmqlwo ."nck"rc|ucti vw"pq"ickuocu0

---

10.   RC™K"RKGUCTF\ DCU"RCU MWOK."K\P EKPQV"PGK\NKGVQV U"\ NGU"XCK" K\OCPVQVQU"OCVGTK NWU."MCU"DKLW™K"UCUMCT "CT"™ O"\ N O."LC" RKGO TQLCOU

---

11.   TG KUVT EKLCU"CRNKGE DCU RC™PKGMC"PQUCWMWOU"WP"CFTGUG

UHN"Rjctocegwvkecnu"Fgwvuejncpf" I odJ
Octkg-Ewtkg-Uvtcuug" :
9;75;"N¾ttcej
X eklc

---

12.   TG KUVT EKLCU"CRNKGE DCU"PWOWTU*-I)

GW13I42I36:7I223

---

13.   U TKLCU"PWOWTU

U tklc

---

14.   K\UPKGI™CPCU"M TV DC

---

37)   PQT F LWOK"RCT"NKGVQ™CPW

---

38)   KPHQTO EKLC"DTCKNC"TCMUV

Rcocvqlwou"Dtcknc"tcmuvc"pgrkgo tq–cpck"kr"cruvkrtkp vu0

---

17.   WPKM NU"KFGPVKHKMCVQTU – 4F"UX VTMQFU

4F ux vtmqfu."mwt "kgm cwvu"wpkm nu"kfgpvkhkmcvqtu0

---

18.   WPKM NU"KFGPVKHKMCVQTU – FCVK."MWTWU"XCT"PQNCU V"RGTUQPC

PC
UP"
NN

FCVK."MCU"QDNKI VK"L PQT FC"W \"OC\C"K\O TC"VKG™ "KGRCMQLWOC

HNCMQPC"OCT LWOU

---

1. \ W"PQUCWMWOU"WP"KGXCF ™CPCU"XGKFI*

NYXTHRACIS 100 o i l o n"uvgtknu"mqpegpvt vu
qdknvqzczkocd"
k0x0"r e"cv- ckf -cpcu0

---

2. NKGVQ™CPCU"XGKFU

Vkmck"xkgptgk| lck"nkgvq-cpck0

---

3. FGT IWOC"VGTOK ™

Fgt iu"n f|

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4. U TKLCU"PWOWTU

U tklc

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70 UCVWTC"UXCTU."VKNRWOU"XCK"XKGP DW"FCWF\WOU

822 oil8 on

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80 EKVC

B.   NĸGVQ™CPCU"ĸPUVTWMEĸLC

Nkgvq-cpcu"kpuvtwmeklc<"kphqt o eklc"rcekgpvc o

NYXTHRACIS **100 o i1o n"mqpegpvt vu"kph |klw"- fwo c"rcicvcxq-cpck**
qdknvqzczkocd

™ o"| n o"vkgm"rkgo tqvc"rcrknfw"w|tcwf| dc"V f l fk"d u"kgur lco u" vtk"kfgpvkhke v"lcwp mq" kphqt o eklw"rct -q"| w"ftq-wo w0"L u"xctcv"rcn f| v."|k qlqv"rct"lgdm fpqx"tqvcl o" dncmwurct f d o0"Rct vq."m "|k qv"rct"dncmwurct f d o."smcv t"60 rwpmvc"dgkg i u0

Rkt o o u"| w"nkgvq-cpcu"w| o cp ik"k|ncukgv"xkuw"kpuvtwmeklw."lq"v "ucvwt"Lwo u"uxct iw"kphqt o eklw0
- Ucincd lkgv"-q|kpuvtwmeklw#"Kgur lco u."mc"x n m"tq"xclcf| u"p tncu v0"
- Lc"Lwo u"tqfcu"lgdm fk"lcwv lwok."xcke lkgv tuvco."hct o cegvcvo"xck" o gf o uck0
- Lc"Lwo u"tqfcu"lgdm fcu"dncmwurct f dcu."mqpuwnl lkgvkgu"ct tuvv."hct o cegvkv"xck" o gf o uw0 Vcu cvvkgecu"ct w|"kgur lco o"dncmwurct f d o."mcu"pcx o kp vcs -cl "kpuvtwmekl 0"Umcv t"60 rwpmvw0

™cl "kpuvtwmekl "xctcv"w||kp v<

30 Mcu"kt"*NYXTHRACIS* wp"m fco "pqn mco "v s"ukgvq"
40 Mcu"Lwo u"l |kpc"rkt o u"*NYXTHRACIS* nkgvq-cpcu
50 M "nkgvqv"*NYXTHRACIS*
60 Kgur lco u"dncmwurct f dcu"
70 M "w|incd v"*NYXTHRACIS*
80 Kgrcmqlwo c"ucvwtu"wp ekvc"kphqt o eklc

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1. Mcu"kt"*NYXTHRACIS* wp"m fco "pqn mco "v u"ukgvq

NYXTHRACIS ucvwt"cmv xq"xkgnw"qdknvqmucmuk o cdw0"Qdknvqmucmuk o cdu"kt o qpqmqp nc"cpvkxkgnc." rtqvg pc"xgkfu."mcu"rkgucksv u"rkg"dcmv tklcu."mwtc"k|tckus"Ukd tklcu o tk."wp"kpcmvkx v u"k|uvt f vqu" vqmus pwu0

NYXTHRACIS nkgvq"mqr "ct"cpvkdkqvkm o "ck" tuv vw"rkgcwiw-qs"wp"d tpwu."mwtkg o "dcmv tlcu" kggnrq-cpcu"tg|wnv t "kt"Ukd tklcu o tku"*kpjcl eklcs"ec "kgi vs"Ukd tklcu o tku+0"

NYXTHRACIS xct"nkgvqv"ct "vcd."lc"Lwo u"xct vw"d "v"dklwuk"ucumctg"ct"Ukd tklcu o tc"dcmv tkl o "xck" urqt o ."dgv"pcnx"unk o dcs"uko rvqo w."wp lc"pcx"rkgglco c"xck"rkgo tqvc"ekvc" tuv -cpc0

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2. Mcu"Lwo u"l |kpc"rkt o u"*NYXTHRACIS* nkgvq-cpcu

Pgnkgvqlkgv"*NYXTHRACIS* - fqu"icf lwo qu<
- lc"Lwo u"kt"cngt klc"rtgv"qdknvqmucmuk o cdw"xck"m fw"ekvw"*80 rwpmv "okp vq+"-q| w"ucuv xfc w0

Dt fkp lwok"wp"rkgusct f| dc"nkgvq-cp "
Rkt o u"*NYXTHRACIS* nkgvq-cpcu"mqpuwnl lkgvkgu"ct tuvv"xck" o gf o uw<

- lc"Lwo u"*xck"L u w"d tpco +"kt"kgf|kovc"htwmqz|gu"pgrcpgucm dc"*KHP+."mcu"kt"tgvk"ucuvqrco o gp vkumc"unko dc."xck"lc"L uw"d tpu"xckvtu"pgcvct"nkgvqv"ucnfwu"r tvkmcs"rtqfwmvwus"xck f| tkgpwu."lq" vcu"k|tckus"pgncdwo w"xck"xgo -cpw"xck"tcfc"v fcu"pgrcv mc o cs"ugmcus"m "x fgtc"r -cpqs."mw c" mtc o rlwu"xck"ecwvgljw0

Cngt kumcs"tgcmeklcu."mcs"xct"tcsvkgs"r e" tuv -cpcs"ct"*NYXTHRACIS*."fcfkm tv"xct"d v"uo cicu0"Rkt o u" *NYXTHRACIS* nkgvq-cpcu"Lwo us"xct"fqt"cpvkjkuvco kpn d| gmk."nck o c"kp vw"cngt kumw"tgcmeklw"tkumw0

Ekvcs"| ngu"wp"*NYXTHRACIS*
Rcuv uvkgt" tuvco "xck"hct o cegvkvco "rct"xku o | n o."mwtcs"nkgvqlcv."r f l "nckm "gucv"nkgvqlkcs"xck"xct vw" nkgvqv0

Lwou"xct"fqv"cpvkdkqvkmcu"*rkgo tc o ."ekrtqhnqmuce pw+."nck"rcn f| vw" tuv v"kpjcn eklcu"eg "kgi vw"
Ukd tklcu"o tk0

I t vpkge dc"wp"dctq-cpc"ct"mt vk

Lc"L u"gucv"it vpkgeg"xck"dctqlcv"d pw"ct"mt vk."lc"fqo lcv."mc"Lwou"xcv vw"d v"it vpkge dc."xck"rl pqlcv"
it vpkge dw. rktou"-q"| w"nkgvkq-cpcu"mqpuwnv lkgvkgu"ct" tuvw0

Pcx"|kp ou."xck"*NYXTHRACIS* xct"mckv v"l uw"pgf|kow-clco"d tpco0"

Pcx"|kp ou."xck"*NYXTHRACIS* k|fcn u"o vgu"rkgp 0"L u"wp"L uw" tuvu"k|ngoukgv."xck"ft muvcv"dctqv"
d pw"ct"mt vk"r c"*NYXTHRACIS* k|Sq-cpcu0

Vtcpurqtvn f|gm w"xcf -cpc"wp"o gj pkuo w"crmcnrq-cpc

NYXTHRACIS xct"k|tcku v"v fcu"dncmwurct f dcu"m "icnxcuu rgu."tgkdqpku."pqiwtwou"wp vgo-cpc0"Vcu"
xct"kgvgkm o v"L uw"p lw"xcf v"vtcpurqtvn f|gm wu"xck"crmcnrq"o gj pkuowu0

NYXTHRACIS ucvwt"uqtd vw"*G642+

Uqtd vu"ktr"htwmvq|!gus"*ewmurc"xgkfu+"cxqvu0"Lc"Lwou"*xck"L uw"d tpco+"ktr tgvc" gp vkumc"unko dc–
kgf|kovc"htwmvq|!gus"pgrcpguo dc"*KHP+."L uw" tuvu"xct"k|ngo v."mc"L u"*xck"L uw"d tpu+"pgfft muvcv"nkgvqv"
-u|p ngu0"Rcekgpvk"ct"IFN qticpkuo gpxgt"uufcdn v"htwmvq|k."mcu"kt -q"| w"ucuv x ."wp"xct k|tcku v"
pqrkgvpcu"dncmwurct f dcu0

Rktou"ac gocv-u| klguo"ktr ra"l rcuv uvc" tuvm."lc"Lwou"*xck"L uw"d tpcq+"ktr"KHP"xck"lc"L uw"d tpu"
xcktu"pgevgr"nkgvqv"ucnfwu"r tvkmcu"rtqfwmvwu"xck"f| tkgpwu."lq"vcu"k|tcku"unkcw f -w. xgo-cpw"xck"ekvcs"
pgrcp mcocu"uck mckv fgtc"r -cpqu."mw c"rac| cu xck"cwtglqv0

NYXTHRACIS ucvwt"n vtklw

™ u| ngu"ucvwt"o c| m"rct"3 o oqn"p vtklc"*45 o i+"mcvt "*NYXTHRACIS* 8 ol"hncmqn —d v d "v u"kt "
õn vtklw"pgucvwtq-cuö0

3. M "nkgvqv"*NYXTHRACIS*

NYXTHRACIS Lwou"fqu tuvu"xck"o gfo uc"crt 0"L uw" tuvu"xck"o gfo uc"cpt kp u"fgxw."rcocvqlqvkgu"w|"
L uw"*xck"L uw"d tpc+ gtog c"ocuw0

L uw" tuvu."o gfo uc"xck"hctocegkvu"ucicvcxqu | ngu"kph |klck0"
NYXTHRACIS – fwow"kgxcf u"x p ."rctcuvk"L uw"tqo ."; 0 okp -w"knicu"kph |klcu xck"kni mcu *ct"
rknkgpkgo+"nckm 0"*NYXTHRACIS* nkgvq-cpcu"nckm ."m "ct"xkuom|xkgpw"uvwpfw"r c"kph |klcu"L u"
w|tcwf| u0"
Rktou"*NYXTHRACIS* nkgvq-cpcu"L u"rctcvk uc goukgv | ngu"cngt kumw"tgcmeklw"pqx t-cpck"xck"
oc|kp -cpck0"

Lc"Lwou"kt"m fk"lww mkt"rct"-q"| w"nkgvq-cpw."lwv lkgv "tuvo ."hctocegkvco"xck"o gfo uck0

4. Kgur lco u"dncmwurct f dcu

V rcv"m "xkuucu"| ngu."- u"| ngu"xct"k|tcku v"dncmwurct f dcu."mcwv ct "pg"xkukgo v u"k|tcwflcu0

**Pgmcx lqvkgu"rcuv uvgv"ucxco " tvco"xck"rgtuqpcn."mwtc"kgxcfc"kph |klw."lc"pqx tqlcv"m fw"pq"
vwtro m"okp vcl o"dncmwurct f d o‹"**

Pkg|g."k|ukvwm."gnrcu"vt mwou"xck"u m–cpcv–u"ct"d v"cngt kumcu"tgcmeklcu"*rccwiuvkp vcu"lwv dcu+"
rc| o gu0

Ekvcu"*NYXTHRACIS* dncmwurct f dcu‹"

Dkgflk *xct"tcuvkgu"n f|"3"pq"32 eknx mkgo+
- Icnxcuu rgu
- Mngrwu
- U rgu"kph |klcu"xkgv
- Pkg|g."k|ukvwok."vquvctp"pkg|q–k."rkgrcegnvk"k|ukvwok"*p vtgpg+

Tgv m *xct"tcuvkgu"n f|"3"pq"322 eknx mkgo+
- Cngt ukmcu"tgcmeklcu
- Tgkdqpku
- Pglwv iwou
- Tgf|gu"lwv dc"rtgv"ickuow"*hqvqhqdklc+
- Pgrcv mcoc"ucl vc"cwu
- T mngu"mcktkp lwou
- Dcuuu"ck|uo cmwou
- U pwuw"pqurtquvqlwok
- Gnrcu"vt mwou
- U rgu"n r u
- Gm| oc." fcu"nqd –cp u
- Owumw tcwlv –cp u."owumw w"urc|omcu
- Pqiwtwou
- Ftgdw k"*uccwmuv –cp u"ucl vc+
- Fkumqmohqtvc"ucl vc"mt –mwtx "
- Xkur t lcu"u rgu"wp"u rgu."mcu"umct"gmuvtgmkv vgu."mt –mwtxk."flqmnk."owumw w uu."uckvgu."e runcu xck"mcwnwu"
- Rkgv mwou"kph |klcu"xkgv ."u rgu"xck"hngd vu"*kgmckuw–cu"x pcu+

\k q–cpc"rct"dncmwurct f d o

Lc"Lwou"tqfcu"lgek fcu"dncmwurct f dcu."mqpuwmv lgvkgu"ct" tuvv."hct mcegkvv"xck ogf m uw0 Vcu"cvvkgcu"ct w|"kgur lco o"dncmwurct f d o."mcu"pcx"okpvcu–cl"kpuvtwkckl 0"L u"xctcv|k qv"rct" dncmwurct f d o"ct"vkg–k."k| mcpvqlqv"<u>X rkgnklwo</u> okp vq"pcekqp l u|k q–cpcu ukuv mcu" mqpvcmvkphqtm cklw. \k qlqv"rct"dncmwurct f d o."L u"xctcv"rcl f| v"pqftq–kp v"fcwf|"rnc– mw" kphqtm cklw"rct–q| w"fdtq–wow0

70 M "w|incd v"*NYXTHRACIS*

W|incd v"– u|ngu"d tpkgo"pgtgf|co "wp"pgrkgglco "xkgv 0

Pgnkgvqv"– u|ngu"r e"fgt iwoc"vgtok c"dgki o."mcu"pqt f vu"w|"mcuvvgu"wp"oct lwo r e"õFgt iu"n f|ö0"Fgt iwoc"vgtok –"cvvkgcu"w|"pqt f v o pg–cp f f lq"fkgpw0

W|incd v"ngfwuumcr "*4 °C–: ÅE+0"
Pgucuc n f v0
W|incd v"qtk kp lcl "kgrcmqlwo ."nck"rcucti vw"pq"ickuomcu0

R e"cv– ckf –cpcu"kph |klcu"mcu " okum ."hk|km n "wp"okmtqdkqnq kum "uvcdknknkgo gq–cpcu"nckm kt" rkgr f vc: uvwpfcu"ukvcdcu"vgo rgtcv t "*42 °C–47 ÅE+"xck"ngfwuumcr "*4 °C–: ÅE+0

R e *NYXTHRACIS* cv– ckf –cpcu"kph |klcu– kte "| ngu"l kgxcfc"pgmcx lqvkgu."pgxku l w|incd 0" Pgk|ocpvqt u|ngu"l kogv0

8) **Kgrcmqlwo c"ucvwtu"wp"ekvc"kphqto eklc**

Mq"*NYXTHRACIS* ucvwt"
- Cmv x "xkgnc"kt"qdknvqmucmuko cdu0"Mcvtu"m"mqpegpvt vc"ucvwt"322 mg"qdknvqmucmuko cdc0"Xkgpu" 8 m"hncmqpu"ucvwt"822 mg"qdknvqmucmuko cdc0
- Ekvcu"ucuv xfc cu"kt"jkuvkf pu."uqtb vu"*G642+."rqpkuqtb2/G655+."u nuuk dg"*G729+"wp"p vtklc" jkftqmu fu"*G746+0"Umcv v"ct "4) ucfc *NYXTHRACIS* ucvwt"uqtb vwö0

NYXTHRACIS t lcku"k|umcvu"wp"kgrcmqlwou
NYXTHRACIS kt"f|kftu"n f|"qrcnguegpvu."dg|mt uckpu"n f|"ick-k"f|gnvgpuick-k"dr picpk"f|gnvgpu" mqpegpvt vu"- fwo c"rcicvcxq-cpck0
NYXTHRACIS kt"rkgglcmu"kgrcmqlwo .'wur "kt"3 hncmqpu0

Tg kuvt eklcu"crnkge dcu" rc-pkgmu
UHN"Rjctmcegwvkecnu"Fgwvuejncpf" I mdJ
Octkg-Ewtkg-Uvtcuug" :
9;75; "N¾ttcej
X eklc

Tcflqv lu"
CegtvkRjctmc"D0X0
Dquejuvtccv"73
6:33" I E."Dtgfc
P fgtncpfg

™ "nkgvq-cpcu"kpuvtwmelc"r f lo"tgk|k"r tumcv vc
™ u"| ngu"kt"tg kuvt vcu"õk| mwmc"k tv"ö0"Vcu"pq| m ."mc"ucmcr "ct- u"iskm dcu"tgtwmu"wp" vkumw" crvx twmu"f "pcx"dklku"kgup lcmu"kgi v"rknp iw"kphqto eklw"rct- m| n m0
Gktqpcu"\ w"c gpv ic"ikm"icfwr tdcwf u"xjvw"lcwpkgi vq"kphqto eklw"rct- m| n m"wp xcjcf| dcu" icf lcmu "cvlcwpkp u"-q"nkgvq-cpcu"kpuvtwmelwo0

Ekvk"kphqto eklcu"cxqvk
U m mc"kphqto eklc"rct- m| n m"kt"rkgglcmc"Gktqpcu"\ w"c gpv tcu"v mgm c"xkgvp <"
<u>jvvr<llyy y0gmc0gwtqrc0gw</u>0"Vwt"kt ct "ucfvgu"w|"ekv m"v mgm c"xkgvp m"rct-tgt m"unkm d m"wp"vq" tuv -cpw0

™ "nkgvq-cpcu"kpuvtwmelc"kt"rkgglcmc"xku u"GU|GG\"xcnqf u"Gktqpcu"\ w c gpv tcu"v mgm c"xkgvp 0

Rcrknfw"kphqto eklc<"<u>y y y0qdknvqzczkmcd-uhn0gw</u> L kgm cwl"ST"mqfu"

26