

BIOM9541

A YW Ub]Wg'cZh\Y'<i a Ub'6cXm

HYfa 'H\fYY''##'&\$&\$

; fUXI UAY'GWXcc``cZ6]ca YX]WJ`9b[]bYYf]b[]`#`! BGK ``9b[]bYYf]b[]

7 ci fgY'8YHJ]`g

7 fYX]hDc]bmg`*`

Gi a a UfmicZhY'7 ci fgY

9j Yf'k cbXYfYX`lck`@cfX'cZhY'F]b[g'cf'5j UHf'k YfY`WYUHYX3'CF`lck`Uh`YH'g WJb`UbU'mgY`hY V]ca YWU]b]Wg'cZhY]f'a cj Ya Ybmg'hc`ja d'fcj Y'dYfZcfa UbVW'3'CF'UVci h`lck`k YUfUV'Y`hYVX'bc'c[mZ'd\cbY Uddg'UbX'ga Ufh[Ufa Ybmg'WJb`VY'i gYX'hc`XYH'WU'UbX'UbU'mgY'i bghUV'Y`[U]hdUH'fg'UbX`\Y'd`k`]h bYi fc'c[]WU`WcbX]hcbg'k U`_VYH'f3'H\]g`Wci fgY`Wcj Yfg`]b`XYdH`hY'a Yh'cXg'i gYX`]b`hY`UbU'mg]g'cZhY V]ca YWU]b]Wg'cZhY'a i gW`cg_Y'YHU`gmgH'a "A Yh'cXg'hc`UbU'mgY`VcXmgY[a YbhUbX`c`]bh_]bYa Uh]WgZ`c`]bh_]bYh]WgZ'k cf`_UbX`dck YfZ'a i gWY`Zc'fW'g'UbX`UggcV]UH'X`YbYf[mWc'ghk`]`VY`Wcj YfYX"5dd`]W]hcbg'cZ V]ca YWU]b]Wg`]b`W]b]W]Z'cVW`dU]hcbU`UbX`fYW'YU]hcbU`UfYUg'k`]`VY`dfYgYbH'X"< >[\`][\hg`]bW`i XY UWW'gg'hc`B`Yi fcgW]YbVW`F`YgYUfVX`5i ghU`]U]g`ghU]!cZhY!Ufh' 8`a`chcb`WJdh`fY`UV`Zc'f'hY'A`c7`Ud`UV'cfU'hc'fmgYgg]cbg"

7 ci fgY'5]a g

H\Y`U]a g'cZh]g`Wci fgY`UfY`hc.

%`b'fcXi W`gh XYbmg'hc`hY`Z`bXUa YbHU`g'cZUbU'ha mUbX`V]ca YWU]b]Wg`UbX`&`fY`UH`hYgY`hc`a YWU]b]WU`UW]hcbg'hc`XY] Y'cd`U`XYdYf'i bXYfghUbX]b[`cZ`hY`Z]X`cZ\i a Ub'a cj Ya YbhgW]YbVW"

'`"8Y] Y'cd`hY`Z`bXUa YbHU`g'cZ' 8`a`chcb`WJdh`fYZ`[U]hUbU'mg]g`UbX'a i gW`cg_Y'YHU`a`cXY`]b[("`b'fcXi W`gh XYbmg'hc`V]ca YWU]b]WU`UbU'mgYg'i g]b[`XUH`Zca`k`YUfUV'Y`hYVX'bc'c[m`

7 ci fgY`@YUfb]b[`Ci hWca Yg

5Z]f'gi WW'ggZ`mWca d`Yh]b[`h]g`Wci fgYZ'mci`g\ci`X`VY`UV'Y`hc.

@YUfb]b[`Ci hWca Y	95`GHU[Y`%7ca dYH'bW]Yg
%`Gh XYbmg'k`]`VY`UV'Y`hc`i`gY`a`YWU]b]WU`df]bV]d`Yg`hc`UbU'mgY` \i a Ub'a cj Ya Ybh	D9`%&
&`Gh XYbmg'k`]`VY`UV'Y`hc`XYg][`b`UbX`dYfZcfa`Yi`dYf]a`Ybhg`hUh` Yj`U`i`UH`\i a Ub'a cj Ya Ybh	D9`&`%`
'`"Gh XYbmg'k`]`VY`UV'Y`hc`W]h]WU`mUbU'mgY`hY]f`Yi`dYf]a`YbHU` ci`hWca`Yg`]b`hY`VfcUXYf`WcbH]`h	D9`%(`
(`"Gh XYbmg'k`]`VY`UV'Y`hc`Wca`a`i`b]WU]h`hY]f`Z]bX]b[`g`YZZ]W]j`Y`m` i`g]b[`cfU`UbX`k`f]hY`b`a`Yh'cXg	D9`'`&
)`"7`f]h]WU`mY]`U`i`UH`X]ZY`fYbh]mdYg`cZk`YUfUV'Y`hYVX'bc'c[]Yg` i`gYX`Zc'f`UbU'mg]b[` \i a Ub'a cj Ya Ybh	D9`%`"

HYUWX]b[`GhfUH[]Yg`

@YWH`fYg'k`]`VY`XY`]`YfYX`cb`]bY`UbX`]bW`i`XY`WcbW`dhXY]`Y`cda`YbH`dfcV`Ya`'gc`]`b[`UbX`X]gW`gg]cb` gYgg]cbg" `hYgY`k`]`Wcj`Yf`hY`hYcfmigi`ddcf]b[`Yi`dYf]a`YbHU`a`Yh'cXg`UbX`hY`dfUW]WU`fYgYUfVX` dfcV`Ya`g`@UV'cfU'hc'f]Yg`UbX`h`hc]U`g`UfY`XYg][`bYX`hc`Yi`d`U]b`hY`WcbW`dhg`]b'fcXi`WYX`]b`hY`cb`]bY`

5 XX]h]cbU`7 ci fgY`bZcfa Uh]cb

6]ca YW\Ub]Mg`]g`hY`gh XmcZhY`YZYWhcZa YW\Ub]WU`d\Ybca YbU`fZcfW`gZj Y`cW]hYgZ UWW`YfU]cbgZ
YbYf[]YgZ`dck YfZ`a ca YbH\Z`a ca YbH\Z`Z]W]cbZ`ZU]h[i Y`UbX`ZU]i fY`c`b`\i a Ub`VcX]Yg`" #ifY`]Yg`cb`Ub
i bXYfg]UbX]b[`cZa YW\Ub]Mg`UbX`Udd`]Yg`hY`Z bXUa YbH`g`cZa YW\Ub]Mg`hc`hY`g]fi W]i fY`UbX`Z bW]cb`cZ
hY`\i a Ub`VcXm`

6]ca YW\Ub]Mg`]g`i gYX`]b`U`X]j YfgY`fUb[Y`cZX]gW]d`]bYg`]bW]i X]b[`V]c`c[nZ`Yf[cbca]MgZ`Yb[]bYYf]b[Z
d\mg]c`c[nZ`a YX]M]bYZ`UbX`a YW\Ub]WU`d\mg]Mg`" A UbmidfcZYgg]cbU`g`-Yb[]bYYfgZ`XYg][bYfgZ`d\mg]WU`
hYfUd]ghgZ`cfU` UbX`cfh`cdUYX]Wgi f[YcbgZ`W]fX]c`c[]ghgZ`UbX`UYfcgdUW`Yb[]bYYfg`-i gY`dfUW]WU`
Udd`]W]h]cbg`cZV]ca YW\Ub]Mg`"

6]ca YW\Ub]Mg`\Ug`Udd`]W]h]cb`]b`U`"UfYUg`cZ\YU`h`W]fY`UbX`a YX]WU`dfcV`Ya`gc`j]b[`h`U]fYei]fY
d\mg]WU`a Ub]di`Uh]cb`" #ia UmVY`hY`a U`cf`UfYU`cZV`bW]fb`]b`gca Y`]bghUbW]g`fY"["Uf]Z]W]U`c`]bH`gZ`
dfcg]hY]Mg`UbX`cfh`cgYgZ`a YW\Ub]ga`g`cZd\mg]WU`]b`f`f`c`f`]ha UmVY`U`j]hU`UX`bW]hc`UbchYf`UfYU`fY"["
XYg][b`cZUb`]a d`UbHUV`Y`dUW`a U`Yf`cf`gdYW]U`]ghgi f[]WU`hc`c`g`"

5ggYgga Ybh

5ggYgga YbhHUg_g

5ggYgga YbhHUg_	K Y][\h	8i Y'8UH	Gh XYbh@YUfb]b[Ci hWta Yg'5ggYggYX
C b`]bY'E i]nnYg`	+I	7cbh]bi ci g	%ž' ž)
MUmUbX'6cc'!`C dYbG]a Dcglg`	, I	7cbh]bi ci g	%ž&ž(
GcZk UFY`@UVcfUhc]Yg`	;%\$I	K KYYgK%ž'g%ž+`/'`+`	%ž&ž&ž' ž(

7ca d`Yh]cb`mci`a`i`ghdcgh`h`fY`h`a`Yg`h`c`f`Y`W`j`Y`h`Y`a`Uf`g`Z`c`f`h`j`g`W`a`dcbYbhcZ`h`Y`UggYgga`Ybh`
Dcgh]b[`Z`k`Y`f`h`U`b`h`f`Y`h`a`Yg`k`j`f`Y`g`i`h`b`U`g`W`c`f`Y`c`Z`\$`f`Y`[`U`f`X`Y`g`g`c`Z`h`Y`a`Uf`g`U`g`g`[`b`Y`X`h`c`j`b`X`j`]`Xi`U`
dcg]g`"

5ggYgga`Ybh`(`GcZk`UfY`@UvcfUhc]Yg`

GhUfhXUHy`K`YY`g`%`z`" /`+`

8YhU]`g`.

GcZk`UfY`@UvcfUhc]Yg`dfcj`j`X`Y`mci`k`j`h`U`b`c`d`d`c`f`h`b`j`m`h`c`Y`U`f`b`U`b`X`i`g`Y`mci`f`c`k`b`X`U`h`W`c`Y`W`h`X`Z`f`c`a`
h`Y`h`f`c`h`c`A`c`7`U`d`U`v`c`f`U`h`c`f`m`h`c`U`b`U`m`g`Y`U`b`X`g`a`i`U`h`Y`i`a`U`b`a`c`j`Y`a`Y`b`h`6`f`b`[`mci`f`c`k`b`U`d`h`c`d`
h`W`i`X`Y`g`.

- Gw]b[
- h]YfgY`?`]bYa`U]Vg
- h]YfgY`8`m`b`Ua`]Vg

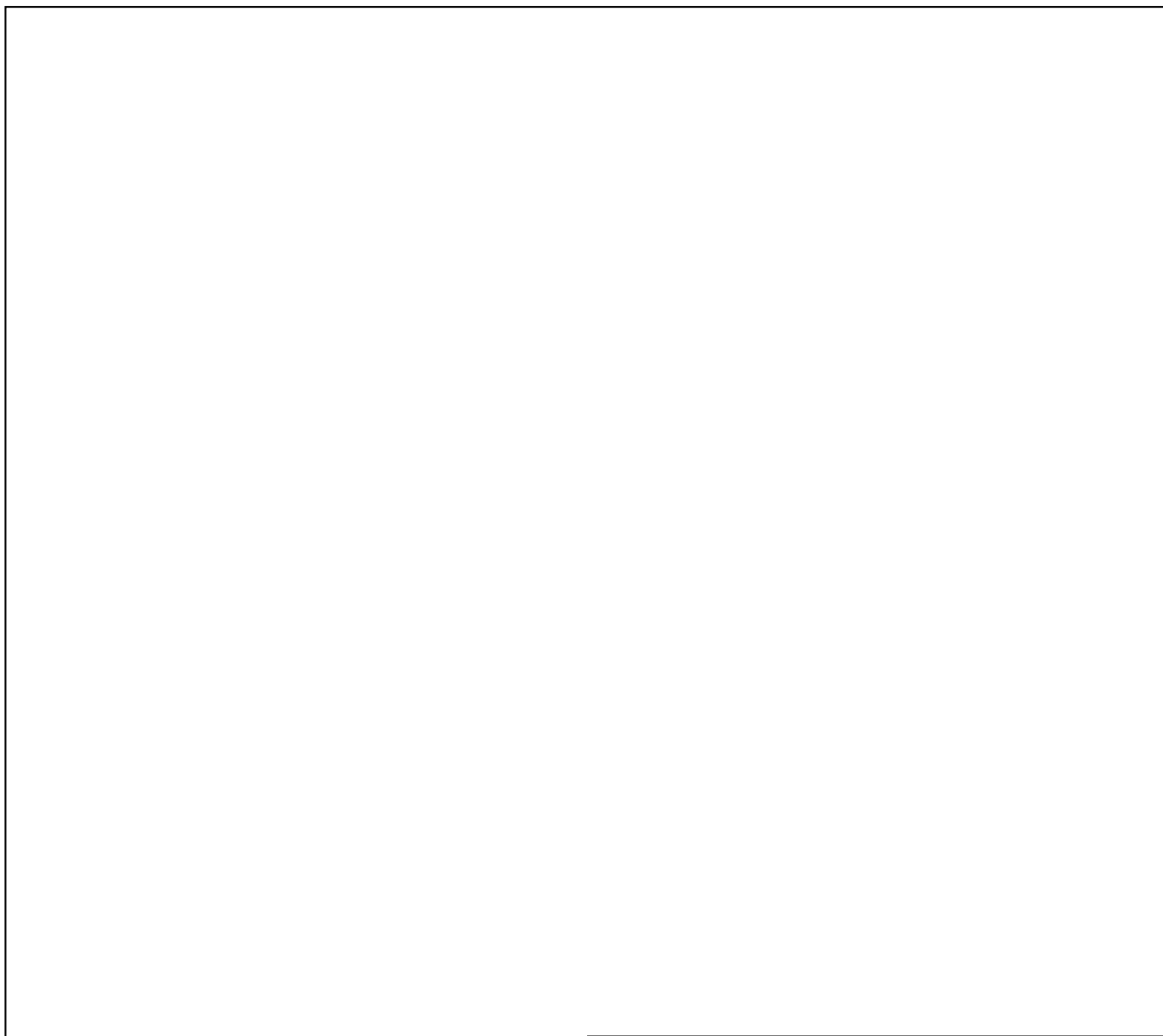
7ca d`Yh]cb`c`Z`U`g`g`Y`g`ga`Y`b`h`]`g`V`U`g`Y`X`c`b`g`c`f`h`k`Y`Y`_`m`X`Y`a`c`b`g`h`U`h`c`b`g`c`Z`mci`f`a`c`X`Y`h`c`mci`f`
X`Y`a`c`b`g`h`U`h`c`f`f`Z`c`f`Z`U`W`h`c`Z`U`W`g`h`i`X`Y`b`h`g`c`f`g`i`V`a`j`h]b[`U`g`W`Y`Y`b`W`U`d`h`i`f`Y`X`Y`a`c`b`g`h`U`h`c`b`f`Z`c`f`Y`a`c`h`
g`h`i`X`Y`b`h`g`c`5`g`c`f`Y`e`i`j`f`Y`g`g`i`V`a`j`h]b[`U`[`f`c`i`d`f`Y`d`c`f`h`c`Z`mci`f`X`j`g`W`g`g`c`b`g`"

5ggYgga`Ybh`(`7ca`di`h]h]cbU`@UvcfUhc]Yg`

GhUfhXUHy`K`YY`g`-`/`%`\$`

8YhU]`g`.

H`Y`c`f`Y`h]W`H`i`h`c`f]U`g`dfcj`j`X`Y`mci`k`j`h`Y`c`d`d`c`f`h`b`j`m`h`c`U`d`d`m`h`Y`h`Y`c`f`m`mci`Y`U`f`b`Y`X`j`b`h`Y`c`b`]b`Y`i`b]g`
X`i`f]b[`k`Y`Y`g`%`z`&`z`" `z`-`/`%`\$`h`c`U`b`U`m`g`Y`h`Y`X`U`h`U`mci`W`c`Y`W`h`X`X`i`f]b[`h`Y`U`v`c`f`U`h`c`f`m`W`U`g`g`]b`k`Y`Y`_`&`" `M`c`i`
k`j`i`g`Y`h`Y`g`Y`X`U`h`U`h`c`W`W`U`h`Y`U`b`X`U`b`U`m`g`Y`U`b`i`a`V`Y`f`c`Z`i`a`U`b`a`c`j`Y`a`Y`b`h`d`U`f`U`a`Y`h`f`g`g`i`W`U`g`c`]b`h`



F Ygci fWg

DfYgWf]VYX`F Ygci fWg`

Gh XYbtg`g\ci`X`Vf]b[`h\Y]f`ck b`Udhd`Wta di hf`hc`GcZk UfY`UbX`7ca di fU]cbU`@UVcfUhc]Yg"

F YWca a YbXYX`F Ygci fWg

H\Y`fYWca a YbXYX`h\i hZcf`h]g`Wci fgY`UFY.

- F cVYf]gcbž8"; "9"YhU`F YgYUfW`a Yhcxg]b`V]ca YWUb]Wg":]fghf`f`gYWcbXE`YX]hcbž<i a Ub ?]bYh]Wgž&\$\$(`f`f`&\$%*`L"
- K]bhYfž8"5"6]ca YWUb]Wg`UbX`a chf`Wcbf`cZ\i a Ub`a cj Ya Ybh`H\]fX`YX]hcbž>c\b`K]Ym/ Gcbgž`bWž&\$\$) "

C h\Yfi gYž`fYZYfbW`Vcc_g`h\UhfY`Y`X`]b`h\Y`I`BGK`@]VfUfmUFY.

- 9bXYfYž>"8"UbX`>"8"6fcbn]bcž`b`f`cXi`W]cb`hc`V]ca YX]W`Yb[]bYYf]b[ž`H\]fX`YX]hcbž5WUXYa]W DfYggž&\$\$&"
- A Yf]Ua ž>"@`UbX`@; "?fU][Yž9b[]bYYf]b[`a YWUb]WgžG] h`YX]hcbž>c\b`K]Ym/ `Gcbgž&\$\$, "

Gh XYbtg`gYY_]b[`UXX]hcbU`fYgci fWg`WUb`Ugc`cVhU]b`Ugg]ghUbw`Zca`h\Y`I`BGK`@]VfUfmUhi
[\hd.##\]VfUfm\]i.bgk`YXi`"Ui`#](#)

5XX]hcbU`fYUX]b[g]UbX`fYWca a YbXYX`k YVg]hYg`k]`VY`]ghYX`cb`A ccX`Y`k`Yb`fYei]fYX"

7ci fgY`9j U`i U]cb`UbX`8Yj Y`cda Ybh

Gh XYbhZYXVUW`Ug`Y`dYX`hc`g`UdY`UbX`XYj Y`cd`h]g`Wci fgYž]bWi`X]b[`ZYXVUW`cVhU]bYX`Zca`cb!]bY`Yj U`i U]cbg`Ug`dUfhcZ]`BGK`g`a`m9]dYf]YbW`dfcW`gg"Mc]f`ZYXVUW`]g`a`i`W`UddfYW]UHYX`UbX`hU`Yb`j`YfmgYf]ci`g`m`7`cb]bi`U`]a`dfcj`Ya`Ybh]UfY`a`UXY`hc`h\Y`Wci`fgY`VUgYX`]b`dUfhcb`gi`W`ZYXVUW`UbX`h]g`Y`dg`i`g`hc`]a`dfcj`Y`h\Y`Wci`fgY`Zcf`Z`h`fY`gh`XYbtg`"bZcfa`U`gh`XYbhZYXVUW`]g`Ugc`gci`[`h`ZYei`Ybh]h]fci`[`ci`h\Y`gYa`YghYf`UbX`i`gYX`hc`Ugg]gh]b`h\Y`dfc[`fYgg]cb`cZ`h\Y`Wci`fgY"

@UVcfUhc]fmK`cf_g`cd`bZcfa`U]cb

Gh XYbtg`k]`VY`fYei]fYX`hc`g][`b`7`C`J`8%`gUZ`XYWUfU]cbg`VYZcfY`UHYbX]b[`UVcfUhc]fmgYgg]cbg"

Gi Va]gg]cb`cZ5ggYgga YbhiHUg_g

@UVcfUhcfmifYdcfhg`UbX`a U`cf`Ugg][ba Ybhg`k]`fYei]fY`U`[Bcb`D`U\[\]Uf\]ga`8YWUfU\]cb`7cj`Yf`G`YYh`](#)

@UH`gi Va]gg]cbg`k]`VY`dYbU`]gYX`%\$i`cZh`Y`a Uf`Zcf`YUW`WJ`YbXUf`XUm`UH`" `Zmc i`ZcfYgYY`U`dfcV`Ya

5 WUXYa]W< cbYgmiUbX`D`U[]Uf]ga

D@5; =F =GA

6Yk UfY`5b`Ugg][ba YbhUUh]bWl XYg`d`U[]Uf]gYX`a UHf]U`k]`fYW]j Y`U`\$i : U]žUbX`gh XYbhtg`k \c d`U[]Uf]gY`a UmZ]j`hY`Wci fgY`Gh XYbhtg`k \c d`U[]Uf]gY`k]`Uj Y`hY]f`bUa Yg`YbHfYX`cb`U`d`U[]Uf]ga fY[]ghf`UbX`k]`VY`]UV`Y`hc`X]gW]d`]bUfmiUW]cbž]bWl X]b[`Yl Wl g]cb`Zca `Ybfc`a Ybh`
#]g`Yl dYWYX`hUUhU`gh XYbhtg`a i ghUUhU`h]a Yg`gi Va]hY]f`ck b`k cf`_`Zcf`UggYgga Ybh`Gi Va]h]b[`hY k cf`_`cf`]XYUg`cZgca YcbY`Y`gY`k]h]ci hWYUfmiUW_bck`YX[]b[`hY`gci fW`cZVcffck YX`a UHf]U`cf`]XYUg`]g d`U[]Uf]ga "

5`UggYgga Ybhtg`k \]Wl`mci `UbX`]b`a i gh`Uj Y`U`[Bcb`D`U\[\]Uf\]ga`8YWUfU\]cb`7cj Yf`G`YYH`H\\]g`\]g`Zcf Vch`\]bX\]j \]Xi U`UbX`\[fci d`k cf`_`5HUVW`\]h\]c`mci f`Ugg\]\[ba YbhVYZcfY`gi Va \]h\]b\[`\]h\]c`hY`7 ci fgY 7 ccfX\]bUhc`f`cf`UhhY`GVXcc`C Z\]W"](#)

D`U[]Uf]ga `]g`hY`i gY`cZUbchYf`dYfgcb`g`k cf`_`cf`]XYUg`Ug`]ZhYmik YfY`mci f`ck b`"K \Yb`]h]g`bYW]ggUfmicf XYg]fUV`Y`hc`i gY`chYf`dYcd`Y`g`a UHf]U`mci `g`ci `X`UXYeI UH`mUW_bck`YX[Y`k \cgY`k cfXg`cf`]XYUg`hYm UfY`UbX`k \YfY`mci `Zci bX`hY`a `f`]j]b[`hY`Wca d`YH`fYZYfYbW`XYH]gž]bWl X]b[`dU[Y`bi a VYffg]H\Y @YUfb]b[`7 YbHfY`dfcj]XYg`Z`fH`Yf`]bZcfa U]cb`cb`k \UhWcbgh]h`H`g`D`U[]Uf]ga `Uh \Hdg`#gh XYbHl bkg "YXi "Ui #d`U[]Uf]ga

5WUXYa]W=Zcfa Uh]cb

7CI FG9'9J5@! 5H€B'5B8'89J9@CDA 9BH

Gh XYbhZYXVUW_\Ug\Y'dYX'hc'g\UdY'UbX'XYj Y'cd'h\]g'Wci fgYz]bWi X]b['ZYXVUW_cVHU]bYX'Zca'cb!
]bY'Yj U'i Uh]cbg'Ug'dUfhcZI BGK 'g'Ug'dUfhcZI BGK 'g'a m9I dYf]YbW'dfcW'gg"Mc'i 'UfY'\][\`m
YbWci fU[YX'hc'Wca d'YH'gi W\ Ub'cb!]bY'Yj U'i Uh]cb'hck UfX'hY'YbX'cZHYfa "': YYXVUW_UbX'gi [[Ygh]cbg
dfcj]XYX'k]"VY']a dcfhUbh]b]a dfcj]b['hY'Wci fgY'Zf'Z hi fY'ghi XYbthg"

85H9G'HC' BCH9

FYZf'hc'A m BGK 'Zcf' a dcfhUbh8UH'gZUj U]UV'Y'Uh
[\hfdg.##a m'i bgk "YXi "Ui #gh XYbh#fYgci fW'g#? Ym8UH'g"\ha`](#)

57589A => '58J =>9

: cf]bZcfa Uh]cb'UVci h

- "B ch'g'cb'UggYgga Ybth'UbX'd'U[]Uf]ga ž
- "GdYV\U'7 cbg]XYfUh]cbgž
- "GWcc"Gh XYbh9h\]W'c Z]W'fz'UbX
- "69GG

fYZf'hc'hY'GWcc'k YVg]H'Uj U]UV'Y'Uh
[\hfd.##k k k "Yb\[\]bYYf\]b\["i bgk "YXi "Ui #/\]ca YX\]WU!Yb\[\]bYYf\]b\#

Gi dd'Ya YbHfM9I Ua]bUh]cbg.

Gi dd'Ya YbHfM9I Ua]bUh]cbg'Zcf'HYfa " '&\$&\$'k]"VY'\Y'X'cb'A cbXUm%#h'>Ubi Ufm-: f]XUm%) h
>Ubi Ufmf]bWi gj YL'g\ci 'X'mci 'VY'fYei]fYX'hc'g]hcbY"

=a U[Y'7 fYX]h

>cgYd\; UthUg'?"fUhcg'cb'hY'gYhcZ"; cX'cZK Uf.'5gW'bg]cb""DcghYX'cb'VY\U'ZcZ>cgYd\; Uth'H\]g
]a U[Y'g'ZYY'hc'i gY'i bXYf'hY'7 fYU]j Y'7 ca a cbg'5hff]Vi h]cb!G\UfY'5'] Y' "\$'I bdcf]YX'W'bgY"

7F =>CG

7F =>CG'Dfcj]XYf'7 cXY.'\$\$\$-; ;

5W_bck`YX[Ya YbhcZ'7ci bHfm

K Y'UW_bck`YX[Y'hY'6YXY[U'dYcd'Y'k \c'UfY'hY'hfUX]h]cbU'W'gfcX]Ubg'cZ'hY'UbXg'cb'k \]W'1 BGK
'?Ybg]b[hc'b'W]a di'g'g'c'W]hYX"

