!" #&/
4;O <548G=>3> 70AB>AC20==O ;V:0@AL:>3> 70A>1C

!®
(AVELOX®)

!:;04:
4VNG0 @5G>28=0: moxifloxacin;

1 D;0:>= (250 <; @>7G8=C)

4>?>28=8: =0B@VN E;>@84, :8A;>B0 E;>@8AB>2>4=520 @>72545=0, =0B@VN 3V4@@>:A84, 2>40 4;O V= T:FV9.

V:0@AL:0 D>@<0. >7G8= 4;O V=DC7V9.
A=>2=V DV78:>-EVABV: ?@>7>@@89 @>7G8= 6>2B>3> :>;L>@C.

$0@<0:>B5@0?52B8G=0 3@C?0. @>B81=V ?@5?0@0B8 4;O A8AB5<=<>3> 70AB>AC20==O. =B810:B5@V0;L=V 70A>18 3@C?8 EV=>;>=V2. >4 "% J01 M 14.

$0@<0:>;>3VG=V 2;0AB82>ABV.
$0@<0:>48=0<V:0

5E0=V7< 4VW
>:A8D;>:A0F8= ?@83=VGCT 10:B5@V0;L=V B>?>V7><5@07 (-3V@070 B0 B>?>V7><5@070 IV), =5>1EV4=V 4;O @5?;V:0FVW,
B@0=A:@8?FVW B0 @5?0@0FVW 10:B5@V0;L=>W .
$0@<0:>:V=5B8:0/D0@<0:>48=0<V:0
40B=VABL DB>@EV=>;>=V2 7=8I8B8 10:B5@VW 70;568BL 2V4 :>=F5=B@0FVW 70;568BL 2V4 BV45= @5?0@0B>2@VABL, I> >A=>2=8< 287=0G0;L=8< D0:B>@>< 5D5:B82=>ABV T A?V22V4=>H5==O I5N ?V4 D0@<0:>:V=5B8G=>W :@82>W (AUC$_{24}$) B0
5E0=V7< @578AB5=B=>ABV
@578AB5=B=VABL 4> DB>@EV=>;>=V2<65 28=8:0<> 2 @57C;LB0BV ?>V7><5==O IV. =EV<5E0=V7<8 @578AB5=B=>ABV B0 >?>A5@54:>20=89 ?V4?>@V4=0 89 ?@>B5=>=0<0<, I> B0:<6 70ABVW2>;L 70?58G0V @578AB5=B=>ABV 4> DB>@EV=>;>=V2<65 >GV:C@B0=8
DB>@EV=>;>=V2, E0@0:B5@=89 4;O 0=B810:B5@V0;L=8E 70A>1V2, I> =0;560BL 4> V=H8E :;0AV2 0=B81V>B8:V2. V4:@8BC 5D5:B
0=B810:B5@V0;L=89 0:B82=VABL =0 V=H8 :;0A8 0=B81V>B8:V2C.
56>2V 7=0G5==O
;V=VG=0 5D5:B82=VABL V4>2545=0 48O;?>3> 48DC7V9=>3> B5AB0 <>:V4;O>G=><C 73V4=> 7 EUCAST (2@>?59AL:89 :><VB5B GCB;82>ABV 4> 0=B81V>B8:V2)
(01.01.2012):

V:@>>@30=V7<	'CB;8289	578AB5=B=89
Staphylococcus spp.	≤ 0,5 <3/; ³ 24 <<	> 1 <3/; < 21 <<

S. pneumoniae	≤ 0,5 <3/; ³ 22 <<	> 0,5 <3/; < 22 <<
Streptococcus 3@C?8 A, B, C, G	≤ 0,5 <3/; ³ 18 <<	> 1 <3/; < 15 <<
H. influenzae	≤ 0,5 <3/; ³ 25 <<	> 0,5 <3/; < 25 <<
M. catarrhalis	≤ 0,5 <3/; ³ 23 <<	> 0,5 <3/; < 23 <<
Enterobacteriaceae	≤ 0,5 <3/; ³ 20 <<	> 1 <3/; < 17 <<
56>2V 7=0G5==O, =5 ?>2O70=V 7 284>< 10:B5@V9*	≤ 0,5 <3/;	> 1 <3/;

*5 ?>2O70=V 7 2840<8 <56>2V 7=0G5==O 1C;8 287=0G5=V 3>;>2=8< G8=><< =0 >A=>2V A?V22V4=>H5==O D0@<0:>:V=5B8G=8E B0 D0@<0:>:>48=0 40=8E V =5 70;560BL 2V4 4;O >;:@5<8E 284V2. &V 40=V 28:>@8AB>2CNBLAO 4;O 284V2, I> =5 <0NBL V=482V4C0;L=> 287=0G5=8E <56>28E 7=0G5=L, V =5 70AB>A>2CNBLAO 4;O 284V2, C O:8E V=B5@?@5B0FV9=V :@8B5@V28 ?V4;O30NBL :@V<V: 287=0G5==N.

V:@@>1V>;>;;>3VG=0 GCB;82VABL

>H8@@@@>5=VABL =01CB>W @578AB5=B=>ABV 284V;5=8E 284V2 2<>65 20@VN20B8AO 70;56=> 2V4 ABV V G0AC, B>1EV4=0 ;:0 V=D>@<0FV> ?@> @578AB5=B=VABL, >A>1;82> ?@8 ;V:C20==V V0:8E V=D5:FV9. # @07V =5>1EV4=>ABV A;V4 725@=CB8AO 70 :>=AC;LB0FVN4> A?5FV0;VAB02, >;;8 H8@@>5=VABL @578AB5=B=>ABV =01C;0 B0:>3> @V2=O, I> 287=0G5==O 2V4 70AB>AC20==O 70A>1C, ?@8=09<=V I>4> 45O:8E 284V2 28:;8:0NBL A;V2, T AC<=V2=N.

0728G09 GCB;82V 2848 >@@>30=V7V7
<u>5@>1=V 3@078B8282=V >@30=V7V7</u> *Staphylococcus aureus** + *Streptococcus agalactiae* (3@C?0 B) *Streptococcus milleri* group* (*S. anginosus, S. constellatus* B0 *S. intermedius*) *Streptococcus pneumoniae** *Streptococcus pyogenes** (3@C?0 A) *Streptococcus viridans* 3@C?0 (*S. viridans, S. mutans, S. mitis, S. sanguinis, S. salivarius, S. thermophilus*)
<u>5@>1=V 3@0<>=53V82=V >@30=V7V7</u> *Acinetobacter baumanii* *Haemophilus influenzae** *Legionella pneumophila* *Moraxella (Branhamella) catarrhalis**

=05@>1=V >@30=V7<8 *Prevotella* spp. =HV >@30=V7<8 *Chlamydophila (Chlamydia) pneumoniae** *Coxiella burnetii* *Mycoplasma pneumoniae**
848, 4;O O:8E <>6;8289 @>728B>: @578AB5=B=>ABV
5@>1=V 3@078B82=V >@30=V7<8 *Enterococcus faecalis** *Enterococcus faecium**
5@>1=V 3@0<=530B82=V >@30=V7<8 *Enterobacter cloacae** *Escherichia coli**# *Klebsiella pneumoniae**# *Klebsiella oxytoca* *Proteus mirabilis**
=05@>1=V >@30=V7<8 *Bacteroides fragilis**
578AB5=B=V >@30=V7<8
5@>1=V 3@0<=530B82=V >@30=V7<8 *Pseudomonas aeruginosa*
*D5:B82=VABL 4>AB0B=L>NN ?@>45<>=AB@>20=0 C :;V=VG=8E 4>A;V465==OE. + 578AB5=B=89 4> <5B8F8;V=C *S. aureus* 4C65 G0AB> T >4=>G0A=> @578AB5=B=8< V 4> DB>@EV=>;>=V2. # <5B8F8;V=>@578AB5=B=8E *S. aureus* @V25=L @578AB5=B=>ABV 4> <>:A8D;>:A0F8=C AB0=>28BL ?>=04 50 %. #(B0<8, O:V 28@>1;ONBL 15B0-;0:B0<07C @>7H8@5=>3> A?5:B@0 (ESBL), T B0:>6 @578AB5=B=8<8 4> DB>@EV=>;>=V2.

$0@<0:>:V=5B8:0.

A<>:BC20==O B0 1V>4>ABC?=VABL

VA;O >4=>@07>2>W V=DC7VW ?@5?0@0BC C 4>7V 400<3 ?@>BO3>< 1 3>48=8 <0:A8<0;L=0 :>=F5=B@0FVO ?@5?0@0BC 4>AO30TBLAO C :V=FV V=DC7VW V AB0=>28BL ?@81;87=> 4,1 <3/;, I> 2V4?>2V40T WW 71V;LH5==N ?@81;87=> =0 26 % 2V4=>A=> 25;8G8=8 FL>3> ?>:07=8:0 ?@8 70AB>AC20==V ?@5?0@0BC ?5@>@0;L=> (3,1 <3/;). >:07=8: AUC AB0=>28BL 1;87L:> 39 <3*3>4/; ?VA;O 2=CB@VH=L>25==>3> 22545==O V BV;L:8 =57=0G=>N N ?5@528ICT F59 ?0@0<5B@ ?@8 70AB>AC20==V ?@5?0@0BC ?5@>@0;L=> (35 <3*3>4/;) C 2V4?>2V4=>ABV 7 01A>;NB=>N 1V>4>ABC?=VABN, O:0 AB0=>28BL ?@81;87=> 91 %.

@8 2=CB@VH=L>25==>

$0@<0:>:V=5B8:0 T ;V=V9=>N 2 4V0?07>=V 50 - 1200 <3 4;O >4=>@07>2>W ?5@>@0;L=>W 4>78, 4> 600 <3 4;O >4=>@07>2>W 2=CB@VH=L>25==>W 4>78 V 4> 600 <3 4;O 70AB>AC20==O 1 @07 =0 4>1C ?@>BO3><

10 4=V2.

>:A8D;>:A0F8= H284:> @>7?>4V;OTBLAO C ?>70AC48==>AB>@V. 1 T< @>7?>4V;C C @V2=>206=>28BL 1;87L:> 2 ;/:3. 0 @57C;LB0B0<8
4>A;V465=L *in vitro* B0 *ex vivo*, 72O7C20==O 7 1V;;:0<8 AB0=>28BL ?@81;87=> 40 - 42 %, =570;56=> 2V4 :>=F5=B@0FVW ?@5?0@0BC.
>:A8D;>:A0F8= 2 >A=>2=>=>< A8@@>20B:8 :@>2V.
0:A8<@0;L=V :>=F5=B@0FVW 5,4 <3/:3 B0 20,7 <3/; (A5@54=V 35>< 5B@@8G=V 7=0G5==O) A?>AB5@V30;8AO C A;87>2V9 >1>;>=FV 1@@>=EV2 B0
@V48=V 5?VB5;V;V5=>W 28ABV::8, 2V4?>2V4=>=>, G5@57 2,2 3>48=8 ?VA;O ?5@>@@0;L=>=>3> ?@89>78. V4?>2V4=>=0 <0:A8<0;L=0 :@=>F5=B@0FVW 2
0;L25>;O@=8E <0:@>D030E AB0=>28;0 56,7 <3/:3. @V48=0 V H:V@@0=V ?CE8@FV2 :@=>F5=B@0FVW 1,75 <3/; 2V448= ?VA;O 2=CB@V H=L>=>=L=>=>3>
225;5==>. @>DV;L «2V;L=0 :@=>F5=B@0FVW   G0A» 4;O V=B5@AB8FV0;L=>=>W @V48=8 8 T 0=0;>3VG=8< ?@>DV;N 4;O ?;07<8 :@=>2V 7 4>A>3=5==>=<
<0:A8<0;L=>=>W 2V;L=>=>W :@=>F5=B@0FVW 1,0 <3/; (A5@54=V T 35>< 5B@@8G=5 7=0G5==O) ?@81;87=> G5@57 1,8 3>4=8 ?VA;O 2=CB@V H=L>=>3> 225;5==>O ?@5?0@0BC.

>:A8D;>:A0F8= ?V4;O30T 2V>B@@0=AD>@=>@@0FVW II D078 V 282>48BLAO 7 >@30=V7=< =8@<0;L=> (1;87L:>
40 %), 0 B0:>6 V7 :0;>=>2G=><8 <0A0=>W (1;87L:> 60 %) O: C =57A?V;5=V: (1) V 3;N:C@@=V4V2V4V2 (2). M1 V M2 T <5B01>;V7>B>=0=>8 @5;520=B=8<8 @;5:8 4;O =48=8, >18420
2>=8 T 1V;L>< >3>=V:>2> =50:B82=8<8.

V4 G0A 4>A;V465=L *in vitro* B0 ::V=VG=8E 4>A;V465=L D078 =5 A?>AB5@V30;>AO <5B01>;V7>=0=>W D0@@=><0:8:>=:V=0=> :8=0=V:8 <0:@>D0W :8=0<V:8 A8<1V>=8:8 7 V=H8<8
?@5?0@0B0<8, 7040=O=0<8 C 1V;L>< >3>=V:V D078 , 2::N>0=N>8 D50=<5=B8 A8ABV5=8 F8B>E@>=><0;L=>=L=>=> <5B01>;V7>

5@V>4 =0?VV2282545==O <>:A8D;>:A0F8=C 7 ?;07<8 :@=>2V AB0=>28BL ?@81;87=> 12 3>48=. !5@54=V9 2AB0=>2;5=89 7030;L=89 ::V@@5=A ?VA;O 225545==O 400 <3 AB0=>28BL 2V4 179 4> 246 <;/E2.

VA;O 2=CB@V H=L>=>3> 225545==O 2 4>7V 400<3, 282545==O ?@5?0@0BC 7 A5G5N C =57<V=V9 D>@=<V 22 %, 7 :0;>=>2 - 26 %. 82545==O 4>78 (=573> ?@5?0@0BC B0 <5B01>;V7>2) AB0=>28BL 98 % ?VA;O 2=CB@V H=L>=>3> 225545==O ;V:0@AL:>=V3> 70A>1C. 8=0V7089 ::V=VG=0 AB0=>28BL ?@81;87=> 2453 </E2 B0 A2V4G8BL ?@> G0A;>V:2C :0=0;;;F52 @501A@0=FVN ?@5?0@0BC 7 =8@@>2:. !C?CB=5 7 V>:A8D;>:A0F8=>< 22545==O @0;;5@>=5 B0 ?@>15=5F84C =5 7<V=N>2 A8AB5=8 F8B>E@>=><0;L=>=> <5B01>;V7>.

5 28O2;5=> V=4828405;L=>=0 V7<V=0 F0@@=><0:8:8=58:8 (7). V 7=865==>< DC=:FVW =8@>: :;V@5=A 28@>D;>:A0F8=C <>65 7=8628B8AO (3;N:C@@=V4V2) 71V;LHCT0;>AO <0965 2 2,5 @078 (7 :;V@5=A>=0>N =54>AB0B=VAB=N < 30 </E2/1,73 <2).

0=V 4>A;V465=L D0@>:V=58:8, ?@>2545=V 70 CG0AB5N ?0FVT=BV2 7 ?5GV=:=>2N =54>AB0B=VAB=N (:;0A , 70 ::0A8DV:0FVTN '09;40 - N), =5 48;;>AO >AB0B>=N= 287=0G8B8, G8 T O:L 2V4=<V=8ABV C ?0FVT=BV2 V7 ?>@C H5==N DC=:FVVN ?5GV=:8 B0 74>@>28E 4>1@>2>;LFV2. @8F;CV2=0 DC=:FVO ?5GV=:8 1C;0 0=0;>3VG=>N 2 >1>E 3@C?0E. 70:A8<0;L=0 :>=F5=B@0FVO ?@5?0@0BC 7 ?>@C H5==N DC=:FVTN ?5GV=:8 =5<0T.

B@048FV9=>8 4>A;V465==OE 7 282G5==O ?>@V2=>@0=>=>3> 4>A;V465=L :;V=V=V=>V =0548@V5=>=FV9 @5;52>2V< B0 <V6 3@C?0=8 B0:>6. V4<V=8 89 2?;82 =0 F5;L>VV;=V ?0@@0=5B@8 =5 =08;8 A8ABV5=8 F8B>E@>=><0;L=>=> 5D5:B82=VAB=N 28V4B V7 ?>@C H5==N
01> ?@5?0@0B V7<V=8;>AO 70 V=H8=8 ?>:07=8:0=8.

8A>:0V ?@5?0@0BC 4>78 C B@82;>8 (≥ 60 <3/:3), =0 B;V 5D5:B82=5 :@=>F5=B@0FVW C ?;07 :@>2V AB0=>28B;>

≥ 20 <3/;, A?@8G8=O;8 7:07=8:V2 5;5:B@>@5B8=>3@0<8, 0 2 >:@5<8E 28?04:0E 0B@@>DVN AVB:V2:8.

VA;O 2=CB@VH=L>25==>3> 70AB>AC20==O A8AB5<=0 B>:A8G=VABL 1C;0 =091V;LH 28@065=>N ?@8 22545==V<>:A8D;>:A0F8=C H;OE>< 1>;NA=8E V=T:FV9 (45 <3/:3) V =5 2V4

VA;O V=B@@00@@B5@@V0;L=>3> 22545==O A?>AB5@@V30;8AO 70?0;L=VT7H8@@5==O< =0 ?5@@V0@B5@@V0;L=V <O:V B:0=8, I> A2V4G8BL ?@@> B5, I> =5>1EV4=> C=8:0B8 V=B@@00@@B5@@V0;L=>3> 22545==O <>:A8D;>:A0F8=C.

>:A8D;>:A0F8= 28O282AO 35=>B>:A8G=8< ?V4 G0A B5ABV2 in vitro7 28:>@@8AB@00==O< 10:B5@V9 01> :;VB8= AA02FV2. # 4>A;V465==OE in vivo 35=>B>:A8G=VABL =5 2V4AC20==O 4C65 28A>:8E 4>7 <>:A8D;>:A0F8=C. >:A8D;>:A0F8= =5 28O282 :0=F5@@>35===>W 4VW C 4>A;V465==V 7 282G5==O :0=F5@@>35=57C C B20@8=.

C<>20E in vitro<>:A8D;>:A0F8= C 28A>:8E :>=F5=B@@0FVOE 2?;8202 =0 5;5:B@@>DV7V>;>3VG=V ?0@0<5B@@8 A5@@F52>W 4VO;L=>ABV, I><>3:>> 28:;8:0B8 ?>4>2265==O V=B5@@20;C QT.

VA;O 2=CB@VH=L>25==>3> 70AB>AC20==O<>:A8D;>:A0F8=C B20@8=0< C 4>7V 30 <3/:3 H;OE>< V=DC7V9 B@@820;VABN 15, 30 01> 60 E28;8= 2V4 4>265==O V=B5@@20;C QT 2V4 H284:>ABV ABV I> :>@@>:><> G0A V=B5@@20, B> 1V;LH 28@065=<> 1C;> ?>4>2265==O V=B5@@20;C QT. >4>265==O V=B5@@20;C QT =5 A?>AB5@@V30;8 ?@@8 22545==V 4>78 30<3/:3 H;OE>< V=DC7V9 B@@820;VABN 60 E28;8=.

@8 282G5==V 2?;82C <>:A8D;>:A0F8=C =0 @5?@@>4C:B82C DC=:FVN B20@8= 4>2545=>, I> <>:A8D;>:A0F8= ?@@>=8:0T :@@V7L ?;0F5=BC. >A;V48, I> ?@@>2>48;8 =0 B20@8=0E, =5 28O28;8 B5@@0B>35==>W 4VW <>:A8D;>:A0F8=C 01> ?@@>3V@@H5==O D5@@B8;L=>ABV ?VA;O 9>3> 70AB>AC20==O. # B20@8=< <>:A8D;>:A0F8= =57=0G==> 71V;LH5==O G0AB>B8 28?04:V2 204 @@>728B:C E@51B0 B0 @515@@, 0;5 BV;L8 C @07V 70AB>AC20==O 4>78 (20 <3/:3 2=CB@VH=L>25==>), O:0 0A>FVN20;0AO V7 A8;L=8< B>:A8G=8< 2?;82>< =0 >@30=V7< <0B5@V. !?>:A8D;>:A0F8=>AO 71V;LH5==O :V;L:>ABV 28?04:V2 ?>5>5@820==O 203VB@@>728V C B20@8=< =0 D>=V B5;0?52B8G=>W >=F5=B@@0FVW C ?;072V, ?>5>5410G5==>W ?@@8 70AB>AC20==V C ;N48=8.

V4><> I> EV@@>;>3V8, 2 B>

;V=VG=V E0@@0:B5@@8AB8:8.

>:070==O.
53>A?VB0;L=0 ?=52<>=VO.
#A;;04=5=V V=D5:FV9=V 70E2>@@N20==O H:V@@8 B0 ?V4H:V@@0=8E B:0=8=.
>:A8D;>:A0F8= A;V4 70AB>A>2C20B8 BV;L:8 B>4V, :;;8 70AB>AC20==O V=H8E 0=B81V>B8:V>;=8E ?@@5?0@@0BV2, O:V 728G09=> @5:><5=4C>> @@5:><5=4C>N@@> ?@@>32V;52=V;=V 0=B81V>B8:V>;;=AO ;V:C20==O F8E V=D5:FV9, T =54>FV;L=8

!;V4 725@@=CB8 C203C =0 >DVFV9=V V=AB@@C:FVW 7 70AB>AC20==O 0=B81V>B8:V>;=8E 70A>1V2.

@@>B8?>:070==O.
-    V?5@@GC;82VABL 4>><>:A8D;>:A0F8=C, V=H8E 0=B81V>B81V>B8:V2 3@@C?8 DC>=>>>;V>=V>>;V2 01> 1C4L-O:>W 7 4>?>28;

-    ?5@@V>4 203VB=>ABV 01> 3>4C20==O 3@@C44N (482. @@>74V;; «0AB>AC20==O C ?5@@V>4 203VB=>ABV 01> 3>4C20==O 3@@C44N»);
-    ?0FVT=B=8 2V:>< 4> 18 @@>:V2;
-    70E2>@@N20==O/?>B@@518 3VO ACE>68;L 2 0=0<=57V, ?@@>2>70V V7 70AB>AC20==O< E;V=VG=8;=>V2.

V4 G0A 4>A;V=VG=8E B0 :;V=VG=8E 4>A;V465=L ?VA;O 22545==O<>:A8D;>:A0F8= A?>AB5@@V30;8AO 7DV7V>;>3V>=V?0@0<5B@@8 A5@@F52>W 4VO;L=>ABV, I> ?@@>O2;O;8AO C D>@@4>4265==O V=B5@@20;C QT. FVTW ?@@8G8=8 <>:A8D;>:A0F8= ?@@>B8?>:070=89 ?0FVT=B0< V7:

-    2@@>465=8< 01> =01CB8< ?>4>2265==O< V=B5@@20;C QT;
-    ?>@@>CH5==O< 10;0=AC 5;5:B@@>;VBV2, >A>1;82> C 28?04:0E C 28?04:0E V7 28@@046=8< V7 28?04:0E ;V=VG=0C< =5A:>@@>3>20=>W 3V?>:0;VT<VT, 3V?><03=VT<VT

- :;V=VG=> 7=0GCI>N 1@048:0@4VTN;
- :;V=VG=> 7=0GCI>N A5@F52>N =54>AB0B=VABN 7V 7=865==O< D@0:FVW 28:84C ;V2>3> H;C=>G:0;
- A8<0B8G=8<8 0@8B0

>:A8D;>:A0F8= =5 <>6=0 >4==>G0A=> 70AB>A>2C20B8 7 ?@5?0@0B0<8, O:V ?>4>26CNBL V=B5@20; QT (482. B0:>6 @>74V; «70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9»).

'5@57 =54>AB0B=V9 ;:V=VG=89 4>A2V4 70AB>AC20==O <>:A8D;>:A0F8= ?@>B8?>:070=89 ?0FVT=B0< V7 ?>@CH5==O< DC=:FVW ?5GV=:8 (:;0A ! 70 :;0A8DV:0FVTN '09;40-N) B0 ?V428I5==O< @V2=V2 B@@0=A0<V=07

70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9.

<u>70T<>4VO 7 ;V:0@AL:8<8 70A>10<8</u>

5 <>6=0 28:;NG8B8 048B82=89 5D5:B <>:A8D;>:A0F8=C B0 V=H8E ;V:0@AL:8E 70A>1V2, I> 740B8:V 28:;8:0B8 ?>4>265==O V=B5@20;;C QTA. &59 5D5:B <>65 ?@8725AB8 4> @>728B:C H;C=>G:>28E 0@8B<V9;V<>@@>=OK=8 H;C=>G:>2C B0E0:0@4VN B8?C «?V@C5B». 7 FVTN ?@8G8=8 70AB>AC20==O <>:A8D;>:A0F8=C 2 :><1V=0FVW 7 1C4L-O:8< V7 86G5707=0G5=8E ;V:0@AL:8E 70A>1V2 ?@>B8?>:070=> (482. B0:>6 @>74V;; «?@>B8?>:070==O»):
- 0=B80@8B<VG=V 70A>18, 3V4@0@5V70F48=, 487>?V@0<
- 0=B80B8:40@>=8, A>B0;>;, 4>D5B8;V4, V1CB8;V4;
- 0=B8?A8E>B8G=V ?@5?0@0B8 (=0?@8:;04, D5>B70B8=8, ?V<>784, A5@B8=4>;;, 30;>?5@84>;;, AC;L?V@84);
- B@8F8:;VG=V 0=B8456@5A0=B8;
- 45O:V ?@>B81V3:V 70A>18 (A0:2V=02V@, A?0@D:>>:A0F8=, 5@8B@><VF8=, ?5=B0<V48=<;>@C;V9=V ?@5?0@0B8, 7>:A5<0 30;>?5@84);
- 45O:V 0=B83V3B0<V==V 70A>18;
- V=HV ;V:0@AL:V 70A>18 (F5D0@>?@84, 2V=:@8AB8=, 15?@84845;, 48D5=>:V9).

>:A8D;>:A0F8= A;V4 7 >15@56=VABN 70AB>A>2C20B8 @0F5=B0< I> <0NBL 28O2;5=V 70E2>@N20==O, I> <>65CBL 7=86C20B8 @V25=L :0;VN (=0?@8:;04, ?5@5;>28 B0 BV=0AF5=8O, 7@>=1V5 70E2>@N20==O B0 :V7V7<5>:C@C>VO B0 V=HV 70E2>@N20==O), :>@8A8>:A5@>W48, 0B5@8@=84), 01> ?@5?0@0B8, ?>2O70=V 7 7C4ON<8 7 V=HV E@>=VG=V 70E2>@N20==O 1@>=EV8 (C 28A>:V9 4>7V), :>; 7 :V7>28 7 :V:B5207C23V:>22C @>74V: 7:;V=VG=V 70B0:8;87 87C48 :>B0:0@8:5V>>V8.

VA;O 1030B>@>07>2>3> 70AB>A>2C20==O <>:A8D;>:A0F8=C C 74>@>28E 4>1@>2>;LFV2 A?>AB5@V30;8 ?>4>26==O V=B5@20;C QT !max 483>:A8=C ?@81;87C>= =0 30 % 157 2?;82C =0 AUC G8 @V25=L 2:070E>W :82>@W.

V4 G0A 4>A;V465=L 70 CG0AB8 4>1@>2>;LFV2, E2>@8E =0 4V015B, >4=>G0A=5 70AB>A>2C20==O <>:A8D;>:A0F8=C ?5@5@@0;L=> B0 3;V:570;048>2 4> 7=865==O <>:A8D;>:A0F8=C 7=86C=0;V A?>AB5@V30;8 ?@81;87=> =0 21 %. ><1V=>20=5 3;V:572>V 2 :@2V, @V25=L V=AC;V=C). B65, :;V=VG=> 7=0G8<>W 270T<>4VW < =5<0T.

4=>3> =>@<0;V7>20=>3> 2V4=>H5==O ().

>2V4><;5=>, I> CG0AB0 ?@>> 25;8::C :V;L:VABL 28?04:V2 71V;LH5==O 0:B82=>A8B82 ?5G5207C >4=>G0A=5 70AB>A>2C20==O B0:8E ;V:0@AL:8E 70A>1V2, O:V >B@8:C20B8 70A>1 :5=8 ?@>@5;5G=>>B8 <0B5@V0;; O:V ?@>0;V70;8 4B->V;V2C28, 8@;L 0:;5 28:8:0<V 70B0:8:0@48 7 ;V:C20==O # :V7>28 7 A28?04V2, <>6;82> ?>2O70=5 7 B0:88 @87:>0<8. $0:B>@0<8, @87::C C :@8B8G=88 B 28:8?:5V9=V 70E2>@N20==O V 70?0;L=89 ?@>F5A 270AB>A>2C20==O # :;V:V=V4>8 4>1@>2>;LFV2 =0 V;O=8 =86G5 0:8?5G=8E =0 B @875:8:=0 75:7 2C=0:5;V<8B8 :;V=VG=> 7=0G8<>W 270T<>4VW <>:A8D;>:A0F8=C 270T<>4VW 7 >:A8D;>:A0F8=> 15=5DV5, ?5@8>48?B8>V >7 V0F@4B?B5B828, 5;;5DV0A89828, 2V:7>8B5@20;V2 4>102:8, <>@@>=8 ?@8 ?>4=V5=0;5@@>L=>:57 4V;V>>7>7>;:

>:A8D;>:A0F8= *in vitro* V7 70AB>A>2C20==O< D5@<5=BV2 F8B>E@><5@01>WVG=>V270==O=0 270T<>4VO 270T<>4V9 D5@<5=BV2 270T<>4V9 F8B>E@><

<u>70T<>4VO 7 W65N</u>

>:A8D;>:A0F8= =5 2802;O;> ?@8 270AB>A>2C20==V 270T<>4V9 7 W65N, 2:;NG0NG8 <>G5G>=V ?@5?0@0B8 ?@>B8:01.

A>1;82V 70E>48 157?5:8.

48= D;0:>= ?@5?0@0BC ?@87=0G5=89 28:;NG=> 4;O >4=>@07>2>3> 70AB>AC20==O. 528:>@8AB0=89 @>7G8= ?V4;O30T CB8;V70FVW.

AB0=>2;5=>, I> =02545=V =86G5 @>7G8=8 T AC 7 @>7G8=>< 4;O V=DC7V9 <>:A8D;>:A0F8=C

400 <3: 2>40 4;O V=T:FV9; @>7G8= =0B@VN E;>@84C 0,9 %; @>7G8= =0B@VN E;>@84C 1-<>;O@@89; @>7G8= 3;N:>78 5 %, 10 %, 40 %; @>7G8= :A8;VBC 20 %; @>7G8= V=35@0; A;04==V @>7G8=8 =0B@VN ;0:B0BC (@>7G8= %0@B<0=0, ;0:B0B=89 @>7G8= V=35@0).

=DC7V9=89 @>7G8= <>:A8D;>:A0F8=C =5 A;V4 22>48B8 AC 7 V=H8<8 ?@5?0@0B0<8.

5 28:>@8AB>2C20B8 ?@5?0@0B 70 =0O2=>=ABV 2848<8E B25@48E 4>: 01> C @07V ?>7G8=C.

@8 715@V30==V C ?@>E>;>4=><5=4CTBLAO 715@V30B8 V=DC7V9=89 @>7G8= ?@8 B5 C.

A>1;82>ABV 70AB>AC20==O.

5@52038 2V4 ;V:C20==O <>:A8D;>:A0F8=>=<, >A>1;82> C 28?04:C =5BO6:8E V=D5:FV9, =5>1EV4=> >FV=N20B8, 15@CG8 4> C2038 V=D>@@<0FVN, O:0 74V;V.

>4>265==O V=B5@20;C QT_A B0 ::V=VG=V C<>28, 70 O:8E <>6;825 ?>4>265==O V=B5@20;C QT_A

AB0=>2;5=>, I> <>:A8D;>:A0F8= C >:@5<8E ?0FV5=B=B02 ?@8872>48BL 4> ?>4>265==O V=B5@20;C QTA =0 5 5;5:B@>:0@4V>3@0@4>265==O V=B5@20;C QT <>65 71V;LHC20B8AO 7V 71V;LH5==O< :>=F5=B@0FVW C ?;072V ?@8 5?0@0=BC C ?;072V ?@8 8 H284:V9 2=CB@VH=L>25==V9 V=DC7VW. "@B@@8<5=40FV9 I>4> B@@820>?ABV V=DC7VW, O:0 ?>28==0 AB0=>2V?<28 =5<5=H5 60 E28;8=, B0 =5 ?5@528528IC20B8 2=CB@VH=L>=5==C 4>7C 400 <3 1 @07 =0 4>1C. V;LH 45B0;L=> 482. C @>74V;0E «@>B8?>:070==O» B0 «70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4VW».

"5@0?VN <>:A8D;>:A0F8=>=< ?@8?8=0=ONBL ?@8 ?>O2V ?V4 G0A ;V:C20==O A8<?B><V4 1CB8 ?>2O70=V 7 A5@F52>N 0@8B<VVO4 B>3>, G8 ?V4B25@46C5@46CBLAO 45 @57C;LB0B0<8 F5@@5:0B0@VAB85==O @57C;LB0B85===V;

>:A8D;>:A0F8= A;V4 7 >15@56=VAB1 70AB>AB>2C20B8 ?0FV5=B0< V7 A8=4@><>< 2@>46=>3> ?>4>=85==O V=B5@20;C QT< V7 V=4828C0;L=8< ?@4825==O< V=B5@20;C QT <>4828 C=CNBL @>72828B8 0@8B<VW C :2@0;05@40), >A>1;825 8 C @07V =40=8 70 2848B B>:>28 C:070=LO70 225ABV A8=E@>=VY C 70<0;L B0 ;V:0@AL70A8D5=V9 V=DC7VW. V;LH 45B0;L=> 482. C @>74V;0E «@>B8?>:070==O» B0 «70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4VW»). 5?0@0=BC 7 @57C;LB0B0<8 70AB>AC20==O <>:A8D;>:A0F8= C 28?04:C A5@F52>W 0@8B<VW 70A>10<8, O:V ?V4B25@46C5@46CBLAO 45 @57C;LB0B0<8 F5@@5:0B0VAB85== (482. B0 =5>1EV4=> >FV=N20B8 ?5@52038 B0 @878:8).

!;V4 7 >15@56=VAB1 70AB>AC20B8 <>:A8D;>:A0F8= ?0FV5=B0< V7 A8=4@><>< B0 ?5?0B8G=8E ?>@C H5=LA ?@8 28?04:C 2@>46=>3> ?>4>=85==O V=B5@20;C QT< V7 V=4828C0;L=8< ?@0825==O< V=B5@20;C QT< =5>1EV4=> >FV=N20B8 ?5@52038 B0 @878:8 (482. B0 =5>1EV4=> >FV=N20B8 ?5@52038).

6V=>: B0 ?V4B25@46C20==O ?>E8;>3> 2V:C <>:A8D;>:A0F8= A;V4 7 >15@56=VAB1 70AB>AC20B8 ?0FV5=B0< V7 A8=4@><>< 2@>46=>3> ?>4>=85==O V=B5@20;C QT_A, B0:>6 >: <>:A8D;>:A0F8=, B0 >:@5<V ?0FV5=B8 1@0=LO >A>1;825>6 C2038.

V428I5=0 GCB;825AB0VAB85/0;5@3V3=V @570:FVW

>2V4><;N;NBL ?@0 28?04:8 @>7V70 70A>10<8 ?V4B25@46C20==O B0 >:@5<V ?0FV5=B8 =5>1EV4=> >FV=N20B8 ?5@52038 B0 @878:8 70A>10<8 @57C;LB0B8 70A>10<8 70AB>AC20==O <>:A8D;>:A0F8= C 28?04:C ?V4B25@46C20==O B0 >:@5<V ?0FV5=B8 ?@5=0@0B >:>8=V, B0:>6 >: 70AB>AC20B8 <>:A8D;>:A0F8= C 28?04:C ?V4B25@46C20==O. # B0:>6 28?04:0E =5>1EV4=> ?@8?8=8B8 70AB>AC20==O <>:A8D;>:A0F8= A;V4 7 >15@56=VAB B0 >15@56=V 2V4?>2V4=5 ;V:C20==O (=0?@8:;04, B5@0?VN H>:C).

"O6:V ?>@CH5==O DC=:FVW ?5G V=:8

@8 70AB>AC20==V <>:A8D;>:A0F8=C ?>2V4><;O;>AO ?@> 28?04:8 DC;L3> 35?0B8BC, I> <>65 ?@872>48B8 4> @>728B:C ?5GV=:>2>W
=54>AB0B=>=>ABV (2:;NG0NG8 ;5B0;L=V 28?04:8) (482. @>74V; «>1VG=V @50:FVW»). # @07V 28=8:=5==O A83> 35?0B8BC, B0:8E O: 0AB5=VO, I>
H284:> @>72820TBLAO B0 AC?@@>2>46CTBLAO 6>2BO=8F5N, B5<=>N A5G5N, AE8;L=VABN 4> :@@>2>B5G 01> ?5GV=:>:>2>N 5=F5D0;>?0BVN,
?0FVT=B=B0< <@5:><5=4CTBLAO ?@@>:>=AC;LBC20B8AO 7 ;V:0@5< ?5@54 ?@@>4=265==O< ;V:C20==O.
@8 ?>O2V >7=0: ?>@@@CH5==O DC:=:FVW ?5GV=:=:8 =5>1EV4=> ?@@>25AB8 4>A;V465==O DC:=:FVW ?5GV=:=:8.

"O6:V 1C;L>7=V H:V@@=V @50:FVW

V4 G0A 70AB>AC20==O <>:A8D;>:A0F8=C ?>2V4><;O;>AO ?@> 28?04:8 1C;L>7=8E H:V@@=8E @50:FV9, B0:8E O: A8=4@@><< !BV25=A0 - 6>=A>=0 01> B>:A8G=89 5?V45@@<0;L=89 =5:@@>;V7 (482. @>74V; «>1VG=V @50:FVW»). @8 ?>O2V @50:FV9 =0 H:V@@V B0/01> A;87>28E >1>;>=:0E ?0FVT=B0<
@5:><5=4CTBLAO =5309=> @@725@=CB8AO 70 <548G=>N 4>?><>3>N, O:I> =5><5 ?@@>4>265==O ;V:C20==O.

0FVT=B8, AE8;L=V 4> @>728B:C AC4><

V4><<, I> EV=>;>;8 <>6CBL 28:;8:0B8 AC4><8. !;V4 7 >15@565==O< ?@875=0G0B8 WE ?0FVT=B0<, O:V <0NBL AE8;L=VABL 4> AC4><,
D0:B>@@8 @87 @0EC20==O :@8B8G=>3> 7=865==O ?>@@>3C AC4><=>3> =0?040 01> 7=86C20==O AC4><=>3> =0?040 ?@@>2V3. @8 ?>O2V AC4>< =5>1EV4=> ?@8?8=8B8
70AB>AC20==O <>:A8D;>:A0F8=C B0 268B8 2V4?>2V4=8E 70E>4V2.

5@8D5@8G=0 =52@>?0BVO

?0FVT=BV2, O:V >B@8<C20;8, 2:;NG0NG8 <>:A8D;>:A0F8=, 1C;8 70?>2V4><;5=V 28?04:8 A5=A>@@=>W 01> A5=A>@@=>-<>B>@@=>W ?>;V=52@>?0BVW,
I> ?@872>48BL 4> ?0@5AB57VW, 3V?5AB57VW, 4875AB57VW 01> A;01:>ABV. 0FVT=B0<, O:V >B@8<C=CNBL <>:A8D;>:A0F8=, @5:><5=4CTBLAO, @87 @0EC20==O
?>O2V >7=0: =52@>?0BVW 2V=D>@@<C20B8 ;V:0@O ?@> 7<V=8 A8<?B><V2, O: 1V;L, ?5G5==O, ?>:>;N20==O, >=V<V=VABL, >=V<V==O, 7<5=H5==O G?C;8B;V2>ABV, ?5@8D5@8G=0
?>;V=52@>?0BVW (482. @>74V; «>1VG=V @50:FVW»).

50:FVW 7 1>:C ?A8EV:8

A8EV:0 <>:A8D;>:A0F8=C <>65 28:;8:0B8 =0@@CH5==O ?A8EV:8, 2:;NG0NG8<>:A8D;>:A0F8=. # ?0FVT=BV2
28?04:0E 45?@@5AVW G8 ?A8EV:0 <>:A8D;>:A0F8=C ?@>28;8AO 4> @>728B:C ACWF840;L=8E 4C<>: 01> ?>2>4V=:8 B0:>3> AV2, O: A@><>28I5 2V4<>28, O: A?@>18 A0<>3C18AB20 01>
>A3C3C1AB20 (482. @>74V; «>1VG=V @50:FVW»). /:I> C ?0FVT=B0 >728820NBLAO B0:V A8<?B><8, ?>B@V1=> =52V4:;04=>28AO 45?@@5AVW, O:V ?0FVT=B0<, O:V E2>@@V
=0 45?@@5AVN 70 45A8;L=8E <V30=52@>?0BV9, ?@@> A?V2 ?>4V1=8E A8<?B><V2, 70 <538G=>N 4>?><>3>N.

8:=852NO, 0A>F9>20=0 V7 70AB>AC20==O< 0=B818V>B8:V2, 2:;NG0NG8 :>;VB

8?04:8 4V0@5W, 0A>F9>20=>W V7 70AB>AC20==O< 0=B818V>B8:V2 (AA), B0 :>;VBC, 0A>F9>20=>W 3> V7 70AB>AC20==O< 0=B818V>B8:V2 (AA),
2:;NG0NG8 ?A524><<5<1@0=>7=89 :>;VB B0 4V0@5N, 0A>F9>20=C 7 *Clostridium difficile* A?>AB5@V30;8AO C 72O7:C V7 70AB>AC20==O<
<>:A8D;>:A0F8=C H8@>:>3> A?5:B@0 4VW, 2 B>2C0@0E 2C:C20==O 9<>2=0?0ABL B0:>3> 4V03=>7C C ?0FVT=BV2, C >B@8<5:<0NBL ?V4 G0A 01> ?V4A;O
<>:A8D;>:A0F8=C <>:A8D;>:A0F8=C >B@8<C20;8 >7=6:8 4V0@5W. @8 ?V427V@65==V 01> ?V42V4B20 B0:8E A8<?B><V2, O: AC4>=8 4V0@5W AA01> AA;V:=C0NBL V7
<>:A8D;>:A0F8=< ?@>=0?81=8E 70A>1V2, 2:;NG0NG8 <>:A8D;>:A0F8=, A;V4 ?@8?8=8B8 B0 68B8 7=865=> ?@@>?V4?>2V4=V 70E>48 @87@0EC20B8 B5@0?V9B0G=G9V=9
70E>48. @8V< FL>3>, =5>1EV4=> 268B8 2V4?>2V4=8E 70E>4V2, A?@>=V;>20=8E =0 :>@@5:FVN 2>4=> :>;5:B@>;VB=>3> 10;0=AC, 7<5=H5==O 1V;:0 @0FV>=V =0?V42 WW ?5@5540GV.
<>:A8D;>:A0F8=<, C >B@8<C20NBL <>:A8D;>:A0F8=C H8@>:>3> A?5:B@0 4VW, ?@>?V4?@>2>4V=V ?@@5?0@0B8, I> ?@83V4=VGCNBL ?5@@8AB0;LB8:C.

0A>F9>20=0, ?>2O720=0 7 B0AC

>:A8D;>:A0F8= A=5 V4: 7 @0EC20==O< B0?@@> <>:A8D;>:A0F8=C ?@>?V4?@>2> 7 B0AC:>N *myasthenia gravis*), >A:V;L:8 2>=0 <>65 7V1V;LHC20B8 A8<?B><8 <VOAB5=VW.

2@V40==O 2>:05>?V8:0, @87 @0EC20==O 2>:05>?V8:V2

V4 G0A 20AB>AC20==O EV=>;>?V8V2 A?>AB5@V30;>AO @V4:5, B0 C B52:>28 28?04:8 :0@4V>20A:C;O@=8E ?>@@CH5=L, O: ?>@@CH5==O @8B<C, ?>2O720=8E 7 @0EC20==O< B0 ?>2O720=8E V7 70AB>AC20==O< <>:A8D;>:A0F8=C, C 28?04:0E ?5@5:@8G=8E B0 A8=5@@3V0;L=8E >B@8<C20G2, 2:;NG0NG8 5?V45@@<0;L=V :0@4V>?>B>:8. V=D>@@<C20B8 ?0FVT=BV2 ?@> 10;>=:0 65?V0:0F, V>4=> ?0B>;>3VG=V 7<V=8 AC4>6NV.

0FVT=B8 7 ?>@CH5==O< DC:FVW =8@>:

0FVT=B0< ?>E8;>3> 2V:C, O:V <0NBL @>7;048 7 1>:C =8@>:, A;V4 7 >15@56=VABN ?@87=0G0B8<>:A8D;>:A0F8=, O:I> 2>=8 =5 A?@@><>6=V ?V4B@@81AO3 @V48=8 2 >@30=V7A:V;L:8 7=52>4=5==O 71V;LHCT @878: 28=8:=5==O =8@@:>2>W =54>AB0B=>>ABV.

>@CH5==O 7 1>:C >@30=V2 7>@@C
@07V ?>3V@H5==O 7>@@C 01> 1C4L-O:>3> 2?;82C =0 >@30=8 7>@C =5>1EV4=> =5309=> 725@@=CB8AO 70 :>=AC;LB0FVTN 4> ;V:0@@O->DB0;L<>;><;>30 (482. @>74V;;8 «40B=VABL 2?;820B8 =0 H284:VABL @50:FVW ?@8 :5@C20==V 02B>B@@@0=A?>@B>< 01> @>1>BV 7 V=H8<8 <5E0=V7<7<0<8», «>1VGG=V @50:FVW @50»).

8A3;V:5
/: V ?@8 70AB>AC20==V 2AVE DB>@@EV=>;;=V2, ?V4 G0A ;V:C20==O<>:A0F8=O<:A0F8=>>< ?>2V4><;>:A0F>V =28?04:8 2V4E8;5;5;==O 2V4 => 07@8 >;>28: C 283;>@V4V 3V@>3;V:5@@72820;0O ?5@520206=> C ?0FVT=BV2 ;VB=L>3> 2V:C, E2>@@8E =0 4V01VB, O:V >@B@@@0=A0@V8=>>:A0F8=>>< ?V4P>@>0;L=V 3V@>3;V:518 (=0?@8:;04, AC;L@0=>V;;;AV4, 3;V28=B=5=<) 01> V=AC;V=. %20@8<< =0 FC:@>289 4V@V5B5B @>5;5> <5=4CTBLAO @5B5L;=> :=>@V=B20=8 @V25=L 3;V>:5=878 2 :@>2V (482. @>74V; «>1VG=V @50:FVW @50»).

@>DV;>0:B8:0 @50:FVW D>B>>A5=A8B8;V70FVW0
V4 G0A 70AB>AC20==O EV=>;;=V2 C ?>0FVT=BV2 @5TAB@@020;8AO >@F0FVW D>B>>A5=A8B8;V70FVW. 4>0:, 70 40=8<8 4>A;V465=L, ?@8 70AB>AC20==V <>:A0F8=C @8788< D>B>>A5=A8B8;V70FVW 1C2 =87L:8<5B>20;;8AO >@F>3V< ;V:0@@0A8: F5@5 A>=FL=5;:>30 >A28B;5==O

0FVT=B8, O:V AB@@@0640NBL =0 45DVF8B 3;N:>7>-6-D>A@0DB=V4>-453V4>@35=>078
0FVT=B8 7 =54>AB0B=VABN 0:B82=>AB V 3;N:>7>-6-D>A@0DB=V4>@453V4>35=078, 0 B0:>6 ?0FVT=B8, C O:8E @VO;L=> 7=8865=0 BV;L:VABL F5@L>=8E :;VB8=, ?@8 ?@8=0:5@@>V 70AB>AC20==V 1C;>-@> 0?@8N@@@81 22545==O, >A:V;L:8 2 4V;L=VAB:V V V=4828V4C0;L=8E 28?04:V2 7@@5AB@@@020=0 A?>AB@@0@T0 B5>4C2 70AB>AC20==O B=@V0@5@>V 22545==O 2?545C>AV;L:8 2 4V;L=VAB

0FVT=B8 7V A5F8?8?4V6=8<8 @50:FVO<8 V 270P@V;LV@==O<8 B0 ?>V4>V38>2882>V8>V0=8B8B8B8 >0@5@>V==O 2 >@35=V7<0E
;V=V@V3>0= 5D5:B0V70VABL 70AB>AC20==O<>:A0F8=8 BV;L:V 2 ?>0FVT=BV2 70VAB<@@>V V;V:C20;0:FVW V=4V2V4C0;L=>, ?@>2B>@0 >B 2;0A=8< V;V:0@@5< D>B>>=A8B8;V70FVW0 ?@5>2@A5@@ 70 A>=FL=5;:@@V <G@020;:, =5 2AB@@@V>:=V;:0.

0FVT=B8, 28 4>B@0VN=5>=V;L:>V= 0?@6820==>< A>=;V
V:0@@0L:89 70AB@0V20=1L@V;L:20>=V4V 0?@3;6820>==>< A>=;V, @>28===V 2@>0E>20>2C20B8 F59 D0:B D>0:B.

?;;82 =0 1V2;:>AVB;L B5AB8B8B5A8B8>5AB8B8B8
>@@V:A0F8=V A=>==> 65 2?8V;B020;8 =0 @57CV;LB028 B5A8B8B=8 =0 28:@8AB@00=> V;0:B>7=> @50:FVW 2>>AB0?5=8V=B@0F2V 10:B5@VO<8 Mycobacterium spp. H;>@V=5O< 70 >0@>3V5=5 10:;::B5@@V0 10:B5@VO@0V@F>30>V60=>I> ;:>;>20B8<>:A0F8=>>=.

0FVT=B8 7 V=D5:FVT:0=> B5A8B=8 =B57 A@0B8;>:>:C9B5=8V0?A5@0V?5V5 @?A5@AV4V7=8V0 (MRSA)
>@V:A0F8=V =5 @5:>V@5=4:C2B8<5V4V;5=V>=F5@V0V;>:C20>==O 10:B5@VO;L=8E V=D5:FVO 28:>28 Staphylococcus aureus (MRSA). @8 >@>2V4V==V B5A8B=8 =0 @0B8;>:>:V8 70 >V1@0=8<8 MRSA, @57CV;L02B028 @5@>5AB@@:0V@V2;V=VG=5 7=@05==O 2@5@AV2 V0@5@AV2 0=B0VB0@0V10:B5@VO;5<V=@5@V0V@ (482. @>74V; «@>04;V1:7>0>=F>80==O

0AB>AC20==O C ?5@V>4V 20VVB=V>ABV 2@045=L >B0VV >==O 3@C4=L.

0@V>4 2V3VB=>ABV
57?5:0 70AB>AC20==O <>:A0F8=C V:C20>==O C ?5@V>4V 20VVB=>AVBV 70 0=5 2820G5=0. 57C@V:A0V10:B5V@V0V@L =0 B2@0@8= =0 10:B5@VO1025=L B0V V0@0OB>V;=V4V =0 >0@=5@O@28>0V10:B5@V8 (482. @>74V; «@>04;V1:7>0>=F>80==O V 3@C4=L 70@4C20==8»). @5@AV5@0= 7 70@AV>=> =0 0:28V=> 20VVB=> =8>F5 =B0@AV0 80:@@0V0V>A02>0A@8B8B>=@05V0=8V5@@>@>=A0>10:B5@V00@5=V0, @0V1:>=V05AV8=@87@>0B5@@5A8@V0@9>1V3V:0@5V70@B0VV0V0V>=5@0C20F0@50>==O O: V V0@B57>@5 BV=>V65?@50>==8@0@5VV@00@8B8V 4VB8=V, O:@ @0=0@@0840NBL =0 B2@0@8= =0 10:B5@VO59, O:V >B@@@040NBL =0 4V01VB59, O: 2@0@V0>08>==0 @5>0==>5V>:>A@5>=0@V00V>@50V>AV;V:0@@59 2V@B5@0A>0==V0 B20V8;;0:@@0 4VB8=V

>4C20==8 3@C4L>V

>4C20==8 3@C4L>V

5<0T 40=8E I>4> 70AB>AC20==O ?@5?0@0BC C ?5@V>4 3>4C20==O 3@C44N C 6V=>:. 57C;LB0B8 4>:;V=VG=8E 4>A;V465=L A2V4G0BL, I>
=525;8:0 :V;L:VABL◇:A8D;>:A0F8=C ?@>=8:0:T C 3@C4=5 ◇;>:>. # 72O7:C V7 2V4ACB=VABN 40=8E I>4> 2?;82C =0 =5◇>2;OB, O:8E 3>4CNBL
3@C44N B0 2@0E>2CNG8 5:A?5@@@8<5=B0;L=89 @878: H:V4;82>3> 2?;82C DB>@@EV=>;=C =0 E@OIV AB0B>:52>57@7@V;8E B20@@8=, I> =5ACBL
>A=>2>5 =020=B0065==O, 3>4C20==O 3@C44N ?@@>B8?>:070=5 ?V4 G0A ;V:C20==O◇:A8D;>:A0F8=>< (482. @>74V; «@>B8?>:070==O»).
$5@B8;=VABL
>A;V465==O =0 B20@@8=0E =5 28O28;8 2?;82C =0 D5@B8;=VABL (482. @>74V; «$0@<0:0;>:;VGV3VG=V 2;0AB82>AB8>ABV»).

40B=VABL 2?;820B8 =0 H284:VABL @@50:FVW ?@8 :5@C20==V 02B>B@@0=A?>@B=< 01> V=H8<8 <5E0=V7<0<8.
>A;V465==O 7 282G5==O 2?;82C ◇:A8D;>:A0F8=C =0 740B=VABL :5@C20B8 02B>B@@0=A?>@B=< B0 ?@0FN20B8 7 <5E0=V7<0<8 =5 ?@@>2>48;8AO.
@>B5 DB>@@EV=>;=8, 2.:;NG0NG8 ◇:A8D;>:A0F8=, ◇>6CBL 2?;8820B8 =0 H284:VABL @@50:FVW ?@8 :5@C20==V 02B>B@@0=A?>@B=< @@1>BV
7 V=H8<8 <5E0=V7<0<8, A?@@8G8=ONG8 @@50:FVW 7 1>:C F5=B@0;L=>W =5@2>2>W A8AB5<8 (=0?@8:;04, 70?0◇>@@>G5==O, 3>AB@@0 B820 2B@@0B0
7>@C) 01> 3>AB@@0C B0 :>@@B:>B@@0B@@820;C 2B@@0BC A2V4><>ABV (=5?@8B><=VABL◇<=VABL), (482. @>74V; «>1VG=V @@50:FVW»). 0FVT=B>@◇ @5:>
<5=4CNBLAO ?@5?5V@@8B8 A2>N @@50:FVN =0 ◇:A8D;>:A0F8= ?5@54 B8<, O: :5@C20B8 02B>B@@0=A?>@B=< 01> ?@0FN20B8 7 <5E0=V7<0<8.

!?>AV1 70AB>AC20==O B0 4>78.
>7C20==O
5:><5=4>20=89 @568< 4>7C20==O 400 <3 ◇:A8D;>:A0F8=C C 283;O4V V=DC7VW 1 @07 =0 4>1C.
>G0B:>20 2=CB@@VH=L>25==O B5@0?VO <>65 1CB8 ?@@>4>265=0 H;OE>< ?5@@>@@0;L=>3> 70AB>AC20==O B01;5B>: ◇:A8D;>:A0F8=C 400 <3 70 C
◇>28 =0O2=>ABV ◇;V=V:>-8=B5@@VG=8E ?>:070=L.
E>4V ◇;V=V:>-8=B5@@VG=8E 4>A;V465=L 1V;LH>VABL ?0FVT=BV2 ?5@@5E;0 =0 ?5@@>@@0;L=8 H>OB50AB>AC20==O ◇:A8D;>:A0F8= ?@@>BO3>< 4 4=V2
(=53>A?VB0;L=0 ?=52◇>=VO) 01> 6 4=V2 (CA:;04=5=0 V=D5:FVO 70E2>@@N20==O H:V@@8 B0 ?V4H:V@@=8E B:0=8=). 5:><5=4>20=0 7030;L=0
B@@820;VABL 2=CB@@VH=L>W 4V V =0O2=>W B5@0?VW ;V:C20==O ◇;V=V:>-8=B5@@VG=8E 7-14 4=V2 4;O =53>A?VB0;L=8E ?=52◇>=V9 B0 7-21 4V2 4;O
CA:;04=5=8E V=D5:FV9=8E 70E2>@@N20=L H:V@@8 B0 ?V4H:V@@=8E B:0=8=.
!?>AV1 70AB>AC20==O
@570@0@0 22>48B8 2=CB@@VH=L>25==> C 283;O4V **157?5@5@@2=>W V=DC7VW B@@820;VABN =5<5=H5 60 E2** (B0:>6 482. @>74V; «A>1;82>ABV
70AB>AC20==O»).
0 =5>B;04=CN @0@5:FVN ?@@>B8>:C @@50:FVN C V=DC7VW >6=0 22>48B8 G5@@57 "-?>4V1=89 :0B5B5@@ @07>< V7 AC
>@CH5==O DC=:FVW =8@@>:
0FVT=B>@, O:V <0NBL ?>@CH5==O DC=:FVW =8@@>:, ?@8: 2V4 ;53:>3> 4> 25@<V@=>3> AB5?5=N, @07 ?0FVT=B>@, @07 E0@@0:B5@@8 B8GV=V?@8:0B>, B0 ?0FVT=B>@, O:V ?5@@51520NBL =0 4V0;V7V, >7C20==O :>@@8@@N20==O 4>78 =5 ?>B@@V1=5 (1V;LH 4>:;04=> 482. C @>74V;V «A>1;
28 =0O2=>ABV»).
!B>A>2=> ?>7C20==O ?0FVT=B0< 7 ?>@CH5==O DC=:FVW 25@<V@=>W B0 28@0065=>W AB5?5=N, @O@07V=< A:<5=5 ?@@518<0NG8 =0 4V0;V7V.

A>1;82>ABV 70AB>AC20==O ?@@>B8>:C
0FVT=B0< ?>4;VB=L>W 2V:C B0 E2V@@>@@8< =0 E>4> 03>AB@@N B8GV V=D5:FVW =5 @5:>@◇5=4>20=5 70AB>AC20==O ◇:A8D;>:A0F8=C.

VB8.
# 72O7:C 7 =530@B82=8< 2?;82>< =0 E@OIV ◇>;>48E B20@@8= (482. @>74V; «$0◇@<0:>:070==O» O: ?@@8 V=DC7VW◇:A8D;>:A0F8=C
4VB8=0 (2V:>◇ 4 18 @>:V2) ?@@>B8>:070=5 (482. @>74V; «@>B8>:070==O»).
D5:B82=VABL B0 157?5:0 70AB>AC20==O ◇:A8D;>:A0F8=C 4VB8=0 B0 ?V4;VB:0< =5 2AB0=>2;5=V (482. @>74V; «@>B8>:070==O»).

5@54>7C20==O.

5 @5:><5=4>20=> ?@>2545==O A?5FV0;L=8E 70E>4V2 ?VA;O 28?04:>2>3> ?5@54>7C20==O. # @07V ?5@54>7C20==O ?@>2>4OBL A8<0B8G=5 ;V:C20==O. A:V;L:8<>6;825 ?>4>265==O V=B5@20;C QT, ?>B@V1=> ?@@>2548B8 -<>=VB@>@8=3. 4=>G0A=5 70AB>AC20==O 0:B82>20=>3> 2C3V;;O V7 4>7>N <>:A8D;>>:A0F8=C 400 <3, I> 1C;0 22545=0 ?5@@0;0>;=> 01> 2=CB@@@VH=L>25==>, 4>72>;;8BL 7<5=H8B8 A8AB5<C 1V>4>ABC?==V=VABL ;V:0>@AL:>3> 70A>1C =0 ?>=04 80 % 01> 20 % 2V4@?>2V4=>. @89><0:B82>20=>3> 2C3V;;O =0 ?>G0B>2V9 AB04VW 01A>@@1FVW<>65 1CB8 5D5:B82=>N ?@@>DV;0:B@V>0:B@V;=V =04;8=H>2>3> 71V;LH5==O A8AB5<0<5=>W 5:A@>78FVW <>:A0F0:A0F8=C C 28?04:0E ?5@54>7C20==O ?VA;O ?5@5>@L>3> ?@89>3> 70A>1C.

>1VG=V @50:FVW.

86G5 =02545=V ?>1VG=V @50:FVW @50:FVW @5>4VN, I> A?>AB5@V30;8A>;8@V6AO C E>4V 4V8:V=V=VG=8;V9 V7 70AB>A0>=>==V<< <>:A0F0:A0F8=C 2 4>7V 400 <3 =0 4>1C (;8H5 2=CB@@@VH=L>25==0 B5@0?VW, ABC?@>0?V=>G=5@<0B0:V =0B>@@VW [2=CB@@@VH=L>25==0/ ?5@@@>@L>;=0] B0 ?5@@@>@L>;=0), B0 WE G0AB>B0. @@>1VG=V @50:FVW @50:FVW @5>4VN, 70 28=OB:>< =0B0:B82@>2;0=B=@>A;V8<><>2>N, A?>AB5@V30;8A>;8;>G 70AB>A@>N@8B0;L=>N<5=>25==0 3 %.

?V:6=V9 3@C??V =0 51060=@ O28I0 287=0G5=@> G5@@V C ?>@O4>:C 7=8@6@5==0 WE 4>ABC0?@VV. '0B0:B82>2V 287=0G5=@> B0:>8 G@8A;@> >=>6=0 >1@0@=8:@>: 4C65 G0AB>=1@ (@≥1/100, <1/10), =@5C0AB>=1@ (≥1/1000, <1/100), ?>>4V48=V9 (≥1/10000, <1/1000), @V4:V9 (<1/10000).

!8AB5<0=<0 @30=;0;0	'0@8=@	=@5C0AB>=1@	?>>4V48=V9	V4:V9
=D5:FVW B0 V=20207VW	AC?@5@@-V=D5:FVW, ?>2O70=V97 @5@3578AB5;0-=8<8 10:B5@V70<8 01> 3@81:0<8, =0?@8:;04 >@0;L=89 B0 203V=0;L=89 :0=484>7			
1>:C >V@>2>=<0<:>8N B0 ;V<@VABV=8 A8AB5<<		0=5@5@V:O, =59B@>@>?5=V:O, B0@><1@>F8B@>@=5=V:O, B@><1>F8B578=>;V:O, ?>4>265==O ?>4>265==O 2V@4>3V9 G0AB>@0F/71V;LH5==0		?V428I5==O @V2=O ?@@>4C:B@>V1@ <5B01>;V:< 5>@L> , @03@0;=L>:;>F@B0@V;>7
1>:C >V@>2>=<8 A8AB5<8		0;5@3V:O=@8 @50:FVW @5>4VN (482. @>7V4V;	0B0:B82=>0=<0 A8AB5<0, 7@3>B>25==07 V=B>@:A@8:0FVW @V4:@V2A@>V2	

>@CH5==O <5B01>;V72>3> AB0BCAC		«A>1;82>ABV 70AB>AC20==O») 3V?5@;V?V45	28?04:0E H>:, I> 703@>6CT 68BBN (482. @>74V; «A>1;82>ABV 70AB>AC20==O»), 0;5@3VG=89 =01@O:/0=3V>=52@>B8G=89 =01@O: (2:;NG0NG8 =01@O: 3>@B0=V, I> ?>B5=FV9=> 703@>6CT 68BBN (482. @>74V; «A>1;82>ABV 70AB>AC20==O») 3V?5@3;V:5	3V?>3;V:5
A8EVG=V @>7;048		@50:FVW AB@82>65=>ABV, ?V428I5==O ?A8E> <>B>@=>W 0:B82=>ABV/ 71C465==O	;01V;L=VABL =0AB@>N, 45?@5AVO (C @V4:VA=8E 28?04:0E 7 <>6;82>N A0 <>03@5AVTN, I> ?@>O2;OTBLAO O: ACWF840;L=V V45W/ 4C A?@>18 A0 <>3C1AB20) (482. @>74V; «A>1;82>ABV 70AB>AC20==O»), 30;NF8=0FVW	45?5@A>=0;V70FVO, ?A8E>B8G=V @50:FVW (7 <>6;82>N A0 <>03@5AVTN, I> ?@>O2;OTBLAO O: ACWF840;L=V V45W/ 4C A?@>18 A0<>3C1AB20) (482. @>74V; «A>1;82>ABV 70AB>AC20==O»)
1>:C =5@2>2>W A8AB5<8	3>;>2=89 1V;L, 70?0 <>@>G5=-=O	?0@5AB57VW / 4875AB57VW, ?>@CH5==O A<0:C	3V?5AB57VO, ?>@CH5==O =NEC (2:;NG0NG8	3V?5@5AB57VO

		(2:;NG0NG8 03527VN C @V4:VA=8E 28?04:0E), A?;CB0=VABL A2V4><>ABV B0 2B@0B0 >@VT=B0FVW, @>7;048 A=C (?5@5206=> V=A><=VO), B@5<B<>@@, 25@B83>, A>=;82VABL	2B@0BC =NEC), ?0B>;>3VG=V A=>284V==O, ?>@CH5==O :>>@48=0FVW (2:;NG0NG8 @>7;04 E>48 2=0A;V4>:: 70?0<>@G5==O 01> 25@B83>), AC4><=V =0?048 (C B> grand mal» =0?048) (482. @>74V; «A>1;82>ABV 70AB>AC20==O»), ?>@CH5==O C2038, @>7;04 <>2;5==O, 0<0=57VO, ?5@8D5@8G=0 =59@>?0BVO B0 ?>;V=59@>?0BVO	
1>:C >@30=V2 7>@C		?>@CH5==O C2038 7>@C, 2:;NG0NG8 48?;>?VN B0 @>7;04 48>7=0==O		@50:FVW 7V=8F, (482. @>74V;8 «A>1;82>ABV 70AB>AC20==O» (>A;V?;5==O) ?V4 G0A =0?04V2
		7>@C (>A;V?;5==O) ?V4 G0A =0?04V2 (482. @>74V; «A>1;82>ABV 70AB>AC20==O»)		(482. @>74V;8 «A>1;82>ABV 70AB>AC20==O», «40=V VABL 2?;828 =0 7404=VABL :5@C20B8 02B><>1V;5< B0 :5@C20==O V=H8<8 <5E0=V7<0<8»)

1>:C >@30=V2 A;CEC B0 25AB81C;O@-=>3> 0?0@0BC 1>:C A5@FO	?>4>265==O V=B5@20;;C QT C E2>@@8E V7 3V?>:;VT 74V;8 «@>B8?>:-70==O», «A>1;82>>ABV 70AB>AC20=-=O»)	?>4>265==O V=B5@20;;C QT (482. @>74V; «A>1;82>>ABV 70AB>AC20==O»), ?>A8;=5 A5@@F518BBO, B0EV:0@4VO, DV1@8;>FVO ?5@54A5@4L, AB5=>>20@4VO	472V= C 2CE0E, ?>@CH5==O A;CEC 2;NG0NG8 3;CE>B0 (70728G09 >1>@>B=>=5?) H;C=>:>2V V2B0EV 2C0B5H <=VABL (=0?8;:8, 3>AB@0B @0 B0 >:@5<;0 2B8>@> <>ABV)	=5A?5F8DVG=V 2@0@B8@>AB V:V@>:>20;NG8«?V@@F5B=0» H;C=>:>2V 20 2C0B5H:0F:0 (« torsade de pointes») (482. @>74V; «A>1;82>>ABV 70AB>AC20==O»), 7C?8=:0 A5@FO (482. @>74V; «A>1;82>>ABV 70AB>AC20==O»)
1>:C AC48=		207>48;0B0F:0	0@B5@V0;L=0 3V?5@B5=7VO, 3V?5@B5=7VO	
1>:C 48E0;L=5H A8AB5<8, 3@C4=5H :;VB:8 B0 >@30=V2 A5@54>ABV==O		7048H:0 (2:;NG0NG8 70AB<VG5=89 A5@F5)		
1>:C H;C=:>2>-:8H:>2>3> B@0:BC	=C4>B0, 1;N20==O, 1V;L C H;C=:>2>-:8H:>2><C B@0:BV, 4V0@5O	7=865==O 0?5B8BC B0 7<5=H5==O <0A8 B5;0 W6V, 70?>@, 48A?5?AVO, D;0BC;5=FVO, 30AB@8B, ?V428I5==O @V2=O	48A>304VO, AB><0B8B, 0A>FFV2>20=89 V7 70AB<VG5==O< C< 2@0B5H:0F:0 :>;VB (2:;NG0NG8 ?A524>;51@0=>7=89 :>;VB, I> C @V4:VH =0?04:0E <>65 70:V=G8B8AO 28?04:0<8 2@0B5H:0F:0 703@>7;8289 4;O 68BB0	

5?0B>1V;V0@=V ?>@CH5==O	?V428I5==O @V2=O B@0=A0	?>@CH5==O DC=:FVW ?5GV=:8 (2:;NG0NG8 ?V428I5==O @V2=O (;0:B0B453V4@>35=0-78)), ?V428I5==O @V2=O 1V;V@C1V=C, "(30< <0-3;CB0W D>AD0B078 :@>2V	68BBO CA:;04=5==O<8) (482. @>74V; «A>1;82>ABV 70AB>AC20==O») 6>2BO=8FO, 35?0B8B (?5@5206=> E>;5AB0B8G=89)	DC;L <>65 ?@8725AB8 4> @>728B:C =5157?5G=>W 4;O 68BBO ?5GV=:82>W =54>AB0B>=>ABV (482. @>74V; «A>1;82>ABV 70AB>AC20==O»)
1>:C H:V@@8 B0 ?V4H:V@@=>W :;VB;8;028=:>W ?V4A>V98=O		A25@1V6, 28A8??0==O, :@>?82O=:0, ACEVABL H:V@@8		1C;L>7=V H:V@@=V @50:FVW O: B0<4@>< !BV25A=A0 - 6>=A>=0 01> B>:A8G=89 5?V45@<0;L=89 =5:@>;V7 (I> ?>B5=FV9=> 703@>6CNBL 68BBN) (482. @>74V; «A>1;82>ABV 70AB>AC20==O»)
1>:C >?>@=>-@CE>2>W A8AB5<8, A?>;CG=>W B:0=8=8 B0 :VAB>:		0@B@0;;3VW,	B5=48=VB (482. @>74V; «A>1;82>ABV 70AB>AC20==O»), ?V428I5==O <O7>2>3> B>=CAC, AC4>@038 <O7V2, <O720 A;01:VABL	@>7@82 ACE>68;;O (482. @>74V; «A>1;82>ABV 70AB>AC20==O»), 0@B@8B8, ?>A8;5==O @8734:8=O <O7V2 B0 AC3;>1V2 O: A8<?B>< myasthenia gravis» (482. @>74V; «A>1;82>ABV 70AB>AC20==O»)

1>:C =8@>: B0 A5G>284V;L=>-3> B@0:BC		453V4@0B0FVO	?>@@CH5==O DC=:FVW =8@>: (2:;NG0NG8 71V;LH5==O @V2=O 07>BC A5G>28=8 :@>2V B0 :@5@0B8=8=C), =8@:>20 =54>AB0B=VABL (482. @>74V; «A>1;82>ABV 70AB>AC20==O»)	
030;L=V @>7;048 B0 AB0=	@50:FVW C	?>30=5 A0 <>?>GCBBO (?5@5206=> 0AB5=VO 01> 2B> <;N20=VABL), 1>;V (2:;NG0NG8 1V;L C A?8=V, 3@C4=VW ?;VBFV, C 4V;O=FV B070 B0 C :V=FV2:0E), ?>A8;5=5 ?>B>284V;5==O, (B@@><1>F8B-) D;51VB C	=01@@>:	

'0AB>B0 @>728B:C =86G5=02545=8E 5D5:BV2 T 28I>N ?@@8 70AB>AC20==V 2=CB@@VH=L>25==>3> H;OEC 22545==O ?@5?0@0B0BC, =0ABC?=V >N ?5@>>@0@;L=>N B5@0@0?VTN 01> 157 B0:>W.

'0AB>: ?V428I5==O @V2=O 30<<0-3;CB0<V;B@0=A?5@0@08 ?V428I5==O @V2=O 30<<0-3;CB0<V;B@0=A?5@08

5G0AB>: H;CE>2V ?@@8 20 B0EV2V>@0@8BB5=7V=0, =01@@>:, 0A>F>V9>20=89 V7 70AB>AC20==O< 0=B81V>B8:0 :>;VB (2:;NG0NG8 ?A524>><5<1@0=>7=89 :>;VB, C @V4:VAE 28?04:0E 0A>F>V9>20=89 V7 703@>>7;820NG8<8 4;O 68BBO CA:;04=5==O<8, 482. @>74V; «A>1;82>ABV 70AB>AC20==O»), AC4><>V=V =0?048 (C B@><«grand mal» =0?048) (482. @>74V; «A>1;82>ABV 70AB>AC20==O»), 30;NF8=0FVW, ?>@@CH5==O DC=:FVW =8@>: (2:;NG0NG8 71V;LH5==O @V2=O 07>BC A5G>28=8 :@>2V B0 :@5@0B8=8=C),=8@:>20 =54>AB0B=VABL (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).
@V4:VAE 28?04:0E ?VA;O ;V:C20==O V=H8B>@0<8 DB>@@5=>;=VA8=8 >ABBV?>V@2V4<>28 ?@@8 @V7=8E 70E2>@N20==OE, C 0 B><C G8A;V V ?@@8 @V2=V 30;N <>2V ?@@8 ?5@5;V<V 5D5:B8, O:V 2@@>3;O4< <>6CBL B0:>6 28=8:08B8 ?VA;O @V2V G0A DB>@@5=>;=VA8=8<>:@5>V=0A8D8:0FVW, @50:FVW D>B>G4B82>3>AB8 (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).
>2V4><<;5==O ?@> ?V4>7@N20==V ?>1VG=V @50:FVW @50:FVW @50:FVW @50:FVW

>2V4><;5==O ?@> ?V4>7@N20=V ?>1VG=V @50:FVW ?VA;O @5TAB@0FVW ?@5?0@0BC T 206;828. >=8 4>72>;ONBL ?@>2>48B8 157?5@5@2=89
<>=VB>@8=3 A?V22V4==8==O @8ABN B0 @878:0<8 70AB>AC20==O ;V:0@AL:>3> 70A>1C. @0FV2=8:8 A8AB5<8 >E>@>=8 74>@>2O ?>28==V
?>2V4><;OB8 ?@> 1C4L-O:V ?V4>7@N20=V ?>1VG=V @50:FVW.

5AC
5 <>6=0 22>48B8 V=DC7V9=89 @>7G8= <>:A8D;>:A0F8=C >4=>G0A=> 7 V=H8<8 =5 AC
20 %; @>7G8= =0B@VN 3V4@>:0@1>=0BC 4,2 %; @>7G8= =0B@VN 3V4@>:0@1>=0BC 8,4 %.
&59 ;V:0@AL:89 70AV1 =5 A;V4 7

"5@ABV. 5 @>:V2.

#<>28 715@V30==O.
15@V30B8 2 =54>ABC?=>
15@V30B8 2 ACE>
5 70<<>@>6C20B8!
@5?0@0B ?>28=5= 715@V30B8AL 2 >@83V=0;L=V9=89 C?0:>2FV.

#?0:>2:0.
> 250 <; @>7G8=C C D;O:>=V. > 1 D;O:>=C @07V< 7 V=AB@C:FVNN 4;O <548G=>3> 70AB>AC20==O 2 :0@B>==V9 ?0GFV.

0B53>@VO 2V4?CA:C. 0 @5F5?B>

8@>1=8:.
09T@ $0@<0 , V<5GG8=0 / Bayer Pharma AG, Germany.

VAF57=0E>465==O 28@>1=8:0 B0 04@5A0 20465==O 9>3> 4VO;L=>ABV.
0975@- V;35;L
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