

!" #&/
4;O <548G=>3> 70AB>AC20==O ?@5?0@0BC

&\$!&
(CIPROFLOXACIN)

!;:04:

4VNG0 @5G>28=0: F8?@>D;>:A0F8=;

1 B01;5B:0 D;>:A0F8=C 3V4@>E;>@84C C ?5@5@0EC20==V =0 F8?@>D;>:A0F8=
250 <3;

1 B01;5B:0 D;>:A0F8=C 3V4@>E;>@84C C ?5@5@0EC20==V =0 F8?@>D;>:A0F8=
500 <3;

4>?>28=8: F5;N;>70 :@8AB0;VG=0, :@>E<0;L :0@B>?;O=89, :@>E<0;L :C:C@C47O=89, 3V?@>5;>70
(3V4@>:A8?@>?V;<5B8;F5;N;>70), B0;L:, =0B@VN :@>A:0@<5;>70, <03=VN AB50@0B, :@5<=VN
4V>:A84 :>;>W4=89 1572>4=89, ?>;V5B8;5=3;V:>;L 6000 (<0:@>3>; 6000), B8B0=C 4V>:A84 (171),
?>;VA>@10B 80.

V:0@AL:0 D>@<0. "01;5B:8, 2:@8BV >1>;>=:>N.

\$0@<0:>B5@0?52B8G=0 3@C?0. =B810:B5@V0;L=V 70A>18 4;O A8AB5<=>3> 70AB>AC20==O. @C?0
DB>@EV=>;>=V2.

>4 "J01M A02.

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

>:070==O. 5CA::04=5=V B0 CA::04=5=V V=D5:FVW, A?@8G8=5=V 71C4=8:0<8, GCB;828<8 4>
F8?@>D;>:A0F8=C.

- =D5:FVW 48E0;L=8E H;OEV2: F8?@>D;>:A0F8= <>6=0 @5:><5=4C20B8 4;O ;V:C20==O ?=52
<>=V9, A?@8G8=5=8E *Klebsiella spp.*, *Enterobacter spp.*, *Proteus spp.*, *Escherichia coli*, *Pseudomonas
aeruginosa*, *Haemophilus spp.*, *Moraxella catarrhalis*, *Legionella*B0 AB0DV;>;>:0<8.
- =D5:FVW A5@54=L>3> 2CE0 (A5@54=V9 >B8B) B0 ?@840B:>28E ?07CE =>A0 (A8=CA8B),
>A>1;82> V=D5:FVW, A?@8G8=5=V 3@0<=530B82=8<8 >@30=V7<0<8, 7>:@5<0 *Pseudomonas
aeruginosa*, 01> AB0DV;>;>:0<8.
- =D5:FVW >G59.
- =D5:FVW =8@>: B0/01> A5G>282V4=8E H;OEV2.
- =D5:FVW AB0B528E >@30=V2, 2;:NG0NG8 04=5:A8B, 3>=>@5N B0 ?@>AB0B8B.
- =D5:FVW >@30=V2 G5@52=>W ?>@>6=8=8 (=0?@8::04, V=D5:FVW H;C=:>2>-.8H:>2>3>
B@0:BC, 6>2G>282V4=8E H;OEV2, ?5@8B=>VB).
- =D5:FVW H:V@8 B0 <O:8E B:0=8=.
- =D5:FVW :VAB>: B0 AC3;>1V2.
- !5?A8A.
- =D5:FVW 01> 28A>:89 @878: V=D5:FV9 (?@>DV;0:B8:0) C E2>@8E 7 >A;01;5=>N VN A8AB5
<>N (C B>45?@5A0=B0<8 B0 ?@8 =59B@>?5=VW).
- 81V@:>20 45:>=B045?@5A0=B0<8.
- @>DV;0:B8:0 V=20782=8E V=D5:FV9, A?@8G8=5=8E *Neisseria meningitidis*

VB8. ?>:A0F8= <>6=0 70AB>A>2C20B8 4VBO< O: ?@5?0@0B 4@C3>W B0 B@5BL>W ;V=VW 4;O
;V:C20==O CA::04=5=8E V=D5:FV9 A5G>282V4=8E H;OEV2 B0 ?VT;>=5D@8BC, A?@8G8=5=8E
Escherichia coli (C ;V=VG=8E 4>A;V465==OE 2V: 4VB59, O:V >45@6C20;8 ;V:C20==O, AB0=>282 2V4 1
4> 17 @>:V2), 0 B0:>6 4;O ;V:C20==O ;535=528E CA::04=5=L, A?@8G8=5=8E *Pseudomonas aeruginosa* C
4VB59 7 2VAF84>7< (C ;V=VG=8E 4>A;V465==OE 2V: 4VB59, O:V >45@6C20;8 ;V:C20==O, AB0=>282
2V4 5 4> 17 @>:V2).

V:C20==O F8?@>D;>:A0F8=<>6=0 ?@87=0G0B8 BV;L:8 ?VA;O @5B5;L=>W >FV=:8
A?V22V4=>H5==O «@878:-:>@8ABL» G5@57 V<>2V@=VABL @>728B:C ?>1VG=8E 5D5:BV2 7 1>:C
AC3;>1V2 B0/01> =02:>;>AC3;>1>28E B:0=8=.

V:C20==O 4VB59 C @0A;V465=L ?@>2>48;>AO BV;L:8 70 707=0G5=8<8 28I5 ?>:070==O<8. ;V=VG=89
4>A2V4 70AB>AC20==O F8?@>D;>:A0F8=C 4VBO< 70 V=H8<8 ?>:070==O<8 >1<565=89.

=30;OFV9=0 D>@<0 A81V@AL:>W 28@07:8 C 4>@>A;8E B0 4VB59.

=865==O @878:C 28=8:=5==O 01> ?@>3@5AC20==O A81V@AL:>W 28@07:8 ?VA;O 05@>35==>3> :>=B0:BC 7 *Bacillus anthracis*

@>B8?>:070==O. V428I5=0 GCB;82VABL 4> F8?@>D;>:A0F8=C 01> 4> V=H8E EVB5@0?52B8G=8E 70A>1V2 3@C?8 EV=>;>=V2 B0 V=H8E :>=5=BV2 ?@5?0@0BC; >4=>G0A=5 70AB>AC20==O 7 B870=V48=>< G5@57 ;V=VG=> 7=0GCIV ?>1VG=V 5D5:B8 (0@B5@V0;L=0 3V?>B5=7VO, A>=>;82VABL), ?>2O70=V 7V 71V;LH5==O< :>=F5=B@0FVW B870=V48=C C ?;072V; 45DVF8B 3;N:>7>- 6-D>AD0B453V4@>35=078.

!>AV1 70AB>AC20==O B0 4>78.

5>1EV4=> 4>B@8DVFV9=8E @5:><5=40FV9 I>4> =0;56=>3> 70AB>AC20==O 0=B810:B5@V0;L=8E 70A>1V2.

568< 4>7C20==O: O:I> =5 ?@87=0G5=> V=H5, @5:><5=4CNBLAO =0ABC?=V 4>1>2V 4>78: ;O 4>@>A;8E

=D5:FVW 48E0;L=8E H;OEV2 (70;56=> 2V4 BO6:>ABV 70E2>@N20==O V 71C4=8:0)	2 × 500 <3 4> 2×750 <3
=D5:FVW A5G>282V4=8E H;OEV2: 3>AB@V, =5CA;:04=5=V F8AB8B C 6V=>: (?5@54 <5=>?0C7>N) CA;:04=5=V	2×250 <3 4> 2×500 <3 @07>20 4>70 500 <3 2 × 500 <3 4> 2×750 <3
>=>@5O: 5:AB@035=VB0;L=0 3>AB@0 =5CA;:04=5=0	2×250 <3 @07>20 4>70 500 <3
=D5:FVW AB0B528E >@30=V2: =5CA;:04=5=0 3>=>@5O (2;:NG0NG8 5:AB@035=VB0;L=V 2>3=810 V=D5:FVW) 04=5:A8B, ?@>AB0B8B, >@E>5?V4848	1×500 <3 2×500 <3 4> 2×750 <3
V0@5O	2×500 <3
=HV V=D5:FVW (482. «>:070==O»)	2×500 <3
@8 >A>1;82> BO6:8E, =5157?5G=8E 4;O 68BBO V=D5:FVOE, =0?@8;:04, ?@8 @5F8482CNG8E V=D5:FVOE C E2>@8E =0 2VAF84>7 ?@8 V=D5:FVOE :VAB>: V AC3;>1V2 A5?B8F5 ?5@8B>=VBV, 7>:@5<0 ?@8 =0O2=>ABV <i>Pseudomonas, Staphylococcus</i> 01> <i>Streptococcus</i>	2×750 <3
=30;OFV9=0 D>@<0 A81V@AL:>W 28@07:8 (?VA;O :>=B0:BC)	2×500 <3
@>DV;0:B8:0 V=20782=8E V=D5:FV9, A?@8G8=5=8E <i>Neisseria meningitidis</i>	1×500 <3

>40B:>20 V=D>@<0FVO I>4> >:@5<8E 3@C? ?0FVT=BV2

VB8 V?V4;VB:8

• #A;:04=5==O 2VAF84>7C

0O2=V ;V=VG=V V D0@<0:>:V=5B8G=V 40=V A2V4G0BL =0 :>@8ABL 70AB>AC20==O F8?@>D;>:A0F8=C 4;O ;V:C20==O ;535=528E 703>AB@5=L, A?@8G8=5=8E *Pseudomonas aeruginosa* C 4VB59 B0 ?V4;VB:V2 7 2VAF84>7< ;535=L (2V:< 2V4 5 4> 17 @>:V2), 4;O ;V:C20==O CA;:04=5=L 2VAF84>7C ;535=L, A?@8G8=5=8E *Pseudomonas aeruginosa* (4>A2V4 70AB>AC20==O BV;L:8 4VBO< 2V:< 2V4 5 4> 17 @>:V2), C 4>7V 20 <3 F8?@>D;>:A0F8=C/:3 <0A8 BV;0 ?5@>@0;L=> 42VGV =0 4>1C (<0:A8<0;L=0 4>1>20 4>70 1500 <3 F8?@>D;>:A0F8=C).

• #A;:04=5=V V=D5:FVW A5G>282V4=8E H;OEV2 B0 ?VT;>=5D@8B

@8 CA::04=5=8E V=D5:FVOE A5G>282V4=8E H;OE2 B0 ?VT;>=5D@8BV 4>70 AB0=>28BL 10-20<3 F8?@>D;>:A0F8=C/:3 <0A8 BV;0 ?5@>@0;L=> :>6=V 123>48=, 0;5 =5 1V;LH5 <0:A8<0;L=>W 4>78 750 <3.

568< 4>7C20==O 4;O ?0FVT=BV2 ;VB=L>3> 2V:C (> 65 @>:V2)

@8 ;V:C20==V ?0FVT=BV2 ;VB=L>3> 2V:C A;V4 70AB>A>2C20B8 O:>>30 =86GV 4>78 F8?@>D;>:A0F8=C 70;56=> 2V4 ABC?5=O BO6:>ABV 70E2>@N20==O V ;V@5=AC :@50B8=V=C.

568< 4>7C20==O ?@8 ?>@CH5==V DC=:FVW =8@>: 01> ?5GV=:8

4>@>A;8E

• >@CH5==O DC=:FVW =8@>::

?@8 ;V@5=AV :@50B8=V=C 2V4 30 4> 60<;/E2/1,73 <2 (?>20 =54>AB0B=VABL) 01> 9>3> :>=F5=B@0FVW C ?;072V 2V4 1,4 4> 1,9 <3/100 <; <0:A8<0;L=0 4>1>20 4>70 F8?@>D;>:A0F8=C <0T AB0=>28B8 1000 <3 =0 4>1C 4;O ?5@>@0;L=>3> 70AB>AC20==O;

?@8 ;V@5=AV :@50B8=V=C<5=H5 30 <;/E2/1,73 <2 (BO6:0 =8@>:20 =54>AB0B=VABL) G8 9>3> :>=F5=B@0FVW C ?;072V 5:2V20;5=B=> 01> 1V;LH5 2 <3/100 <; <0:A8<0;L=0 4>1>20 4>70

F8?@>D;>:A0F8=C <0T AB0=>28B8 500 <3 =0 4>1C 4;O ?5@>@0;L=>3> 70AB>AC20==O (4;O 2AVE ;V:0@AL:8E D>@<).

• >@CH5==O DC=:FVW =8@>: B0 35<>4V0;V7:

?@8 ;V@5=AV :@50B8=V=C 2V4 30 4> 60<;/E2/1,73 <2 (?>20 =54>AB0B=VABL) 01> 9>3> :>=F5=B@0FVW C ?;072V 2V4 1,4 4> 1,9 <3/100 <; <0:A8<0;L=0 4>1>20 4>70 F8?@>D;>:A0F8=C <0T AB0=>28B8 1000 <3 =0 4>1C 4;O ?5@>@0;L=>3> 70AB>AC20==O;

?@8 ;V@5=AV :@50B8=V=C<5=H5 30 <;/E2/1,73 <2 (BO6:0 =8@>:20 =54>AB0B=VABL) G8 9>3> :>=F5=B@0FVW C ?;072V 5:2V20;5=B=> 01> 1V;LH5 2 <3/100 <; <0:A8<0;L=0 4>1>20 4>70

F8?@>D;>:A0F8=C <0T AB0=>28B8 500 <3 =0 4>1C 4;O ?5@>@0;L=>3> 70AB>AC20==O.

• >@CH5==O DC=:FVW =8@>: B0 E@>=VG=89 ?5@8B>=50;L=89 4V0;V7 2 0<1C;0B>@=8E C <>20E:

?5@>@0;L=5 70AB>AC20==O F8?@>D;>:A0F8=C C D>@:, 2:@8B8E >1>;>=:>N, C 4>7V 1 B01;5B:0 ?> 500 <3 F8?@>D;>:A0F8=C.

• >@CH5==O DC=:FVW ?5GV=:8:

:>@5:FVO 4>78 =5 ?>B@V1=0.

• >@CH5==O DC=:FVW =8@>: B0 ?5GV=:8:

?@8 ;V@5=AV :@50B8=V=C 2V4 30 4> 60<;/E2/1,73 <2 (?>20 =54>AB0B=VABL) 01> 9>3> :>=F5=B@0FVW C ?;072V 2V4 1,4 4> 1,9 <3/100 <; <0:A8<0;L=0 4>1>20 4>70 F8?@>D;>:A0F8=C <0T AB0=>28B8 1000 <3 =0 4>1C 4;O ?5@>@0;L=>3> 70AB>AC20==O;

?@8 ;V@5=AV :@50B8=V=C<5=H5 30 <;/E2/1,73 <2 (BO6:0 =8@>:20 =54>AB0B=VABL) G8 9>3> :>=F5=B@0FVW C ?;072V 5:2V20;5=B=> 01> 1V;LH5 2 <3/100 <; <0:A8<0;L=0 4>1>20 4>70

F8?@>D;>:A0F8=C <0T AB0=>28B8 500 <3 =0 4>1C 4;O ?5@>@0;L=>3> 70AB>AC20==O.

5<0T 4>A2V4C 70AB>AC20==O ?@5?0@0BC 4VBO< 7 ?>@CH5==O< DC=:FVW =8@>: 01> ?5GV=:8.

! ?>AV1 70AB>AC20==O. "01;5B:8 F8?@>D;>:A0F8=C, 2:@8BV >1>;>=:>N, A;V4 :>2B0B8 =5 @>76>2CNG8 V 70?820B8 =525;8:>N :V;L:VABN @V48=8.

"01;5B:8 F8?@>D;>:A0F8=C, 2:@8BV >1>;>=:>N, <>6=0 ?@89<0B8 =570;56=> 2V4 26820==O W6V. 0AB>AC20==O ?@5?0@0BC =0BI5A5@F5 ?@8A:>@NT 70A2>T==O 0:B82=>W @5G>28=8. # B0:>

D;>:A0F8=C, 2:@8BV >1>;>=:>N, =5 A;V4 ?@89<0B8 >4=>G0A=> 7 26820==O< <>;>G=8<8 ?@>4C:B0<8 01> =0?>O<8, 71030G5=8<8 =V, ACBBT2> =5 2?;820T =0 2A<>:BC20==O F8?@>D;>:A0F8=C.

>;8 70E2>@N20==O ?@>BV:0T C BO6:V9 D>@ G5@57 V=HV ?@8G8=8 (=0?@8::04 O:I> E2>@89 >B@8 D;>:A0F8=C. VA;O :C@AC V=T:FV9 ;V:C20==O<>6=0 ?@>4>268B8 V7 70AB>AC20==O< B01;5B>:

F8?@>D;>:A0F8=C.

"@820;VABL ;V:C20==O

"@820;VABL ;V:C20==O 70;568BL 2V4 BO6:>ABV 70E2>@N20==O, ;V=VG=>3> ?5@51V3C B0

10:B5@V>;>3VG=>3> ?@>DV;N. 06;82> ?@>4>26C20B8 ;V:C20==O ?@>BO3< ?@8=09<=V 3 4=V2

?VA;O =>@<0;V70FVW B5 7=8:=5==O ;V=VG=8E A828BL:

• 1 45=L ?@8 3>AB@V9 =5CA::04=5=V9 3>=>@5W B0 F8AB8BV;

• 4> 7 4=V2 ?@8 V=D5:FVOE =8@>;, A5G>282V4=8E H;OE2 B0 >@30=V2 G5@52=>W ?>@>6=8=8;

• 4;O E2>@8E 7V 7=865=8< V< ;V:C20==O 74V9A=N20B8 ?@>BO3< CAL>3> ?5@V>4C =59B@>?5=VW;

- ?@8 >AB5>
- 7-14 4=V2 ?@8 2AVE V=H8E V=D5:FVOE;
- 7030;L=0 B@820;VABL ;V:C20==O ;535=52>W D>@<8 A81V@AL:>W 28@07:8 (?VA;O :>=B0:BC) F8?@>D;>:A0F8=>< (2=CB@VH=L>25==> 01> ?5@>@0;L=>) AB0=>28BL 60 4=V2.

@8 V=D5:FVOE, A?@8G8=5=8E AB@5?B>:>:0<8, ;V:C20==O A;V4 ?@>4>26C20B8 O:
10 4=V2 4;O C=8:=5==O @878:C @>728B:C ?V7=VE CA;:04=5=L.

@8 V=D5:FVOE, A?@8G8=5=8E *Chlamydia*, :C@A ;V:C20==O B0:>6<0T B@820B8 I>=09<5=H5
10 4=V2.

VB8 B0 ?V4;VB:8

- #A;:04=5==O 2VAF84>7C

@8 CA;:04=5==OE 2VAF84>7C ;535=L, A?@8G8=5=>3>*Pseudomonas aeruginosa*, C 4VB59 (2V:< 2V4 5
4> 17 @>:V2) B@820;VABL ;V:C20==O AB0=>28BL 10-14 4=V2.

- #A;:04=5=V V=D5:FVW A5G>282V4=8E H;OE2 01> ?VT;>=5D@8B

@8 CA;:04=5=8E V=D5:FVOE A5G>282V4=8E H;OE2 01> ?VT;>=5D@8BV, A?@8G8=5=8E*Escherichia coli*, :C@A ;V:C20==O AB0=>28BL 10-21 4=V2.

@8 ;V:C20==V ;535=52>W D>@<8 A81V@AL:>W 28@07:8 (?VA;O :>=B0:BC) A?V22V4=>H5==O
«@878:-:>@8ABL» 4>2>48BL, I> 70AB>AC20==O F8?@>D;>:A0F8=C E2>@8< 4VBO< T 4>FV;L=8

>1VG=V @50:FVW.

=D5:FVW B0 V=207VW: 3@81:>2V AC?5@-V=D5:FVW (H:V@=89 :0=484>7; :0=484>7 >@0;L=89,
H;C=>2>-.8H:>289, 203V=0;L=89), 0=B81V>B8:>-0A>FV9>20=89 :>;VB (4C65 @V4:> 7 <>6;82>N
;5B0;L=VABN).

!8AB5<0 :@>2>B2>@5==O B0 ;V: 5>78=>DV;VO, ;59:>?5=VO, 0=5?5=VO, ;59:>F8B>7, B@>
<1>F8B>?5=VO, B@><1>F8B5F8B>7, ?0=F8B>?5=VO (=5157?5G=0 4;O 68BBO), ?@83=VG5==O
:VAB:>2>3> <>7:C (=5157?5G=5 4;O 68BBO), ;V?0BVO, <5B35<>3;>1V=5

: 0;5@3VG=V @50:FVW, 0;5@3VG=89/0=3V>=52@>B8G=89 =01@O; 0=0DV;0:B8G=V @50:FVW,
0=0DV;0:B8G=89 H>: (=5157?5G=89 4;O 68BBO), @50:FVW, ?>4V1=V 4> A8@>20B:>2>W E2>@>18.

A8EVG=V @>7;048: ?A8E>@=0 71C4;82VABL/B@82>6=VABL, A?;CB0=VABL A2V4=>ABV V
457>@VT=B0FVO, ?0B>;>3VG=V A=>284V==O, 45?@5AVO, 30;NF8=0FVW, ?A8E>B8G=V @50:FVW,
?>@CH5==O ?>254V=:8, ACWF840;L=V 4C10 A0<>3C1AB20, <0=V0:0;L=0 @50:FVO, D>1VO,
45?5@A>=0;V70FVO.

5@2>20 A8AB5<0: 3>;>2=89 1V;L, A>;82VABL, @>7;048 A=C, 157A>==O, ;5B0@3VO,
2=CB@VH=L>G5@5?>0 3V?5@B5=7VO, A;01:VABL, ?>@CH5==O :>>@48=0FVW, ?>@CH5==O =NEC
G8 A<0:C, ?0@5AB57VW, 4875AB57VW, 3V?5AB57VW, 3V?5@5AB57VO, B@5>@, AC4<8,
?5@8D5@8G=0 =59@>?0BVO B0 ?>;V=59@>?0BVO.

@30=8 A;CEC: ?>@CH5==O A;CEC, 472V= C 2CE0E, 2B@0B0 A;CEC.

@30=8 7>@C: ?>@CH5==O 7>@C, ?>@CH5==O :>;L>@>2>3> A?@89=OBBO, 7=865==O 3>AB@>B8
7>@C, 42>W==O 2 >G0E, 1V;L 2 >G0E, =VAB03

!5@F5: B0EV:0@4VO, ?>4>265==O V=B5@20;C QT, H;C=>G:>20 0@8BB@V?>BV==O ?5@54A5@4L,
AB5=>:0@4VO, V=D0@:B :0@40, 2V4GCBBO A5@F518BBO, 7C?8=:0 A5@FO.

!C48=8: 207>48;0B0FVO, 3V?>B5=7VO, A8=:>?0;L=89 AB0=, 3V?5@B5=7VO, 20A:C;VB, 35
<>@03VG=89 4V0B57, B@><1>7 AC48= 3>;>2=>3> <>7:C, D;51VB.

@30=8 48E0==O, B>@0:0;L=V B0 <54V0AB8=0;L=V @>7;048: 48A?=>5 (2;:NG0NG8 0AB<0B8G=V
AB0=8), =>A>20 :@>2>B5G0, :@>2>E0@:0==O, 1@>=E>A?07<, =01@O; ;535=L 01> 3>@B0=V, 38:02:0,
;535=520 5<1>;VO.

(;C=:>2>-.8H:>289 B@0:B: 48A?5?A8G=V @>7;048, <5B5>@87<, 0=>@5:AVO, 48AD03VO, =C4>B0,
1;N20==O, 4V0@50, 1V;L C 4V;O=FV H;C=:0 V :8H5G=8:C, ?0=:@50B8B,1>;NGVABL A;87>2>W
>1>;>=8 ?>@>6=8=8 @>B0, ?5@D>@0FVO :8H5G=8:C, H;C=:>2>-.8H:>2V :@>2>B5GV.

5?0B>1V;V0@=0 A8AB5<0: ?V428I5==O @V2=V2 B@0=A0@CH5==O DC=:FVW ?5GV=:8, 6>2BO=8FO,
35?0B8B (=5V=D5:FV9=89), =5:@>7 ?5GV=:8 (4C65 @V4:> B0:89, I> ?@>3@5ACT 4> ?5GV=:>2>W
=54>AB0B=>ABV, O:0 703@>6CT 68BBN).

(:V@0 B0 ?V4H:V@=0 ;:VB:>28=0: 28A8?0==O, :@>?82O=:0, A25@1V6, @50:FVW D>B>GCB;82>ABV, ?>O20=5A?5F8DVG=8E ?CE8@FV2, ?5B5EVW, 5@8B5<0, @<=0 5@8B5<0, 2C7;8:>20 5@8B5<0, A8=4@>< !BV25=A0-6>=A>=0 (7 ?>B5=FV9=>N 703@>7>N 68BBN), B>:A8G=89 5?V45@<0;L=89 =5:@>;V7 (7 ?>B5=FV9=>N 703@>7>N 68BBN), 3>AB@89 35=5@0;V7>20=89 5:70=B5<0B>7=89 ?CABC;L>7, 5:AD>;V0B82=89 45@<0B8B.

!5;5B=>-<O7>20 A8AB5<0 V A8AB5<0 A?>;CG=>W B:0=8=8: 0@B@0;3VW, 8@:8 V A5G>284V;L=V H;OE8: ?>@CH5==O A5G>28?CA:0==O, ?>@CH5==O DC=:FVW =8@>;, =8@:>20 =54>AB0B=VABL, ?>;VC@VO, 35<0BC@VO, F8;V=4@C@VO, :@8AB0;C@VO, BC1C;>V=B5@AB8FV0;L=89 =5D@8B, C@5B@0;L=0 :@>2>B5G0. 030;L=V AB0=8: =5A?5F8DVG=89 1>;L>289 A8=4@><, =574C60==O, 30@OG:0, =01@O:8, ?V428I5=0 ?VB;82VABL (3V?5@3V4@>7), 3V?5@?V3<5=B0FVO, ?>@CH5==O E>48, 703>AB@5==O ?>403@8, 203V=VB, 1V;L C 3@C4=8E 70;>70E. 01>@0B>@=V ?>:07=8:8: ?V428I5==O @V2=O: ;C6=>W D>AD0B078 :@>2V, 0;V?078, B@83;VF5@84V2, 30<<03;CB02V, A5G>2>W :8A;>B8;3V?5@3;V:5 3V?>3;V:5 2V4E8;5==O 2V4 =>@<8 @V2=O ?@>B@><1V=C, 71V;LH5==O 4=>3> =>@<0;V7>20=>3> 2V4=>H5==O () C ?0FVT=BV2, O:V ?@89<0NBL 0=B03>=VAB8 2VB07, 7B@><1V=>2>3> G0AC. * &V @50:FVW A?>AB5@V30;8AO ?5@5206=> C ?0FVT=BV2 7 4>40B:>28<8 D0:B>@0<8 @878:C ?@>;>=30FVW V=B5@20;C QT (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

0ABC?=V =51060=V ?>1VG=V O28I0 <0NBL ?V428I5=C G0AB>BC 28=8:=5==O C ?V43@C?0E ?0FVT=BV2, O:8< 70AB>A>2CNBL ?@5?0@0B 2=CB@VH=L>25==> 01> ?>A;V4>2=> (?VA;O 2=CB@VH=L>25==>3> 2545==O ?5@>@0;L=89 A?>AV1 70AB>AC20==O):1;N20==O, B@0=78B>@=5 71V;LH5==O 0:B82=>ABV B@0=A0B@><1>F8B>?5=VO, B@><1>F8B5<>ABV V 457>@VT=B0FVO, 30;NF8=0FVW, ?0@5AB57VW B0 4875AB57VW, AC4<8, 70?0<>@>G5==O, 2V7C0;L=V ?>@CH5==O, 2B@0B0 A;CEC, B0EV:0@4VO, 207>48;0B0FVO, 0@B5@V0;L=0 3V?>B5=7VO, B@0=78B>@=0 ?5GV=:>20 =54>AB0B=VABL, 6>2BO=8FO, =8@:>20 =54>AB0B=VABL, =01@O:8; ?0=F8B>?5=VO, ?@83=VG5==O :VAB:>2>3><>7:C, 0=0DV;0:B8G=89 H>;, ?A8E>B8G=V @50:FVW, ?>@CH5==O =NEC, ?>@CH5==O A;CEC, 20A:C;VB, ?0=:@50B8B, =5:@>7 ?5GV=:8, ?5B5EVW, @>7@82 ACE>68;L.

0AB>AC20==O 4VBO<. # 4VB59 0@B@>?0BVO A?>AB5@V30TBLAO G0ABVH5 (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

5@54>7C20==O. =0A;V4>: ?5@54>7C20==O ?@8 ?5@>@0;L=>AC20==V C 45O:8E 28?04:0E 2V47=0G0;0AL >1>@>B=0 B>:A8G=0 4VO =0 ?0@5=EV:.">7C20==O, :@V< ?@>2545==O 728G09=8E 70E>4V2 (?@><820==O H;C=:0, 70AB>AC20==O 1;N20;L=8E 70A>1V2, 22545==O 25;8:>W :V;L:>ABV @V48=8, AB2>@5==O :8A;>W @50:FVW A5GV), @5:×5=4CTBLAO B0:>6 AB568B8 70 DC=:FVTN =8@>: B0 ?@89<0B8 0=B0F848, I> >2V4><;O;>AO, I> ?5@54>7C20==O C 4>7V 12 3 ?@872>48;> 4> A8W B>:A8G=>ABV. >AB@5 ?5@54>7C20==O C 4>7V 16 3 ?@872>48;> 4> @>728B:C 3>AB@>W =8@:>2>W =54>AB0B=>ABV. !8<8 ?5@54>7C20==O 2;;NG0;8 70?0<>@>G5==O, B@5<>@, 3>;>2=89 1V;L, 2B<8, 30;NF8=0FVW, A?>CB0=VABL A2V4<>ABV, 014>@B, =8@:>2C B0 ?5GV=:>2C =54>AB0B=VABL, 0 B0:>6 :@8AB0;C@VN B0 35<0BC@VN.

0AB>AC20==O C ?5@V>4 203VB=>ABV 01> 3>4C20==O 3@C44N. ?>:A0F8= =5 <>6=0 70AB>A>2C20B8 203VB=8< V 6V=:0<, O:V 3>4CNBL 3@C44N, 2@0E>2CNG8 2V4ACB=VABL 4>A2V4C 9>3> 70AB>AC20==O FV9 :0B53>@VW ?0FVT=BV2. !?8@0NG8AL =0 40=V 28?@>1C20=L =0 B20@8=0E, =5 <>6=0 ?>2=VABN 28;;NG0B8 V<>2V@=VABL CH:>465==O AC3;>1>28E E@OIV2 C =>2>=0@>465=8E, B>4V O: <>6;82VABL B5@0B>35==8E 5D5:BV2 (<0;LD>@<0FV9) =5 ?V4B25@465=0. 5@V>4 3>4C20==O 3@C44N. ?>:A0F8= ?@>=8:0T C 3@C4=5 <>;>:.'5@57 ?>B5=FV9=89 @878: ?>H:>465==O AC3;>1=8E E@OIV2 C =>2>=0@>465=8E F8?@>D;>;:A0F8= =5 A;V4 70AB>A>2C20B8 ?V4 G0A 3>4C20==O 3@C44N.

VB8.

?>:A0F8= <>6=0 70AB>A>2C20B8 4VBO< O: ?@5?0@0B 4@C3>W B0 B@5BL>W ;V=VW 4;O ;V:C20==O CA:;04=5=8E V=D5:FV9 A5G>282V4=8E H;OEV2 B0 ?VT;>=5D@8BC, A?@8G8=5=8E *Escherichia coli* 0 B0:>6 4;O ;V:C20==O ;535=528E CA:;04=5=L, A?@8G8=5=8E *Pseudomonas aeruginosa* C 4VB59 7 2VAF84>7>

V:C20==O F8?@>D;>:A0F8=<>6=0 ?@87=0G0B8 BV;L:8 ?VA;O @5B5;L=>W >FV=:8 A?V22V4=>H5==O «@878:-:>@8ABL» G5@57 V<>2V@=VABL @>728B:C ?>1VG=8E 5D5:BV2 7 1>:C AC3;>1V2 B0/01> ?@8;53;8E B:0=8=.

;V=VG=89 4>A2V4 70AB>AC20==O F8?@>D;>:A0F8=C 4VBO< 70 V=H8<8 ?>:070==O<8 >1<565=89.

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

"O6:V V=D5:FVW B0/01> V=D5:FVW, A?@8G8=5=V 3@078B82=8<8 01> 0=05@>1=8<8 10:B5@VO<8. ;O ;V:C20==O BO6:8E V=D5:FV9, V=D5:FV9, A?@8G8=5=8E AB0DV;>:>:0<8 01> 0=05@>1=8<8 10:B5@VO<8, F8?@>D;>:A0F8= A;V4 70AB>A>2C20B8 C :<>1V=0FVW 7 2V4?>2V4=8<8 0=B810:B5@V0;L=8<8 70A>10<8.

=52<>:>:8. ?>:A0F8= =5 @5:><5=4CTBLAO 4;O ;V:C20==O ?=52<>:>:28E V=D5:FV9 G5@57 =54>AB0B=N 5D5:B82=VABL I>4> 10:B5@V9 3@C?8 *Streptococcus pneumoniae* =D5:FVW A5G>2>3> B@0:BC. @E>5?V4848@N20==O >@30=V2 <0;>3> B070 <>6CBL 1CB8 28;;8:0=V DB>@>EV=>:>:-@578AB5=B=8<8 *Neisseria gonorrhoeae*. ?>:A0F8= A;V4 ?@87=0G0B8 >4=>G0A=> 7 V=H8<8 2V4?>2V4=8<8 0=B810:B5@V0;L=8<8 ?@5?0@0B0<8, 70 28=OB:>< :;V=VG=8E A8BC0FV9 28;;NG0NG8 F8?@>D;>:A0F8=-@578AB5=B=VE HB0<8 *Neisseria gonorrhoeae*. !:I> G5@57 3 4=V =5 =0AB0T ;;V=VG=5 ?>:@0I5==O, B5@0?VN A;V4 ?5@53;O=CB8.

0=V ?@> 5D5:B82=VABL F8?@>D;>:A0F8=C ?@8 ;V:C20==V ?>AB>?5@0FV9=8E V=B@0014>1<565=V. 0@4V0;L=V ?>@CH5==O. ?>:A0F8= 0A>FVNTBLAO 7 ?>4>265==O< V=B5@20;C QT =0 5;5:B@>:0@4V>3@074V; <>1VG=V @50:FVW». 0FVT=B8 ;VB=L>3> 2V:C<>6CBL 1CB8 1V;LH GCB;828<8 4> 27;82C ?@5?0@0BC =0 V=B5@20; QT. !;V4 7 >15@56=VABN 70AB>A>2C20B8 F8?@>D;>:A0F8= V7 AC?CB=V<8 ?@5?0@0B0<8, O:V <>6CBL A?@8G8=OB8 ?@>:>=30FVN V=B5@20;C QT (=0?@8;;04 0=B80@8B, B@8F8;;VG=V 0=B845?@5A0=B8, <0:@>;V48, 0=B8?A8E>B8:8), B0 E2>@8< V7 D0:B>@0<8 @878:C I>4> 707=0G5=8E AB0=V2 (=0?@8;;04, ?@>:>=30FVO QT 2 0=0 <=57V, =5:>@83>20=0 3V?>:0;VT

VB8 B0 ?V4;VB:8. =0;V7 =002=8E 40=8E I>4> 157?5:8 70AB>AC20==O F8?@>D;>:A0F8=C 4VBO<, 1V;LHVABL V7 O:8E AB@0640;8 =02VAF84>7, =5 =0402 6>4=8E 4>:07V2 ?>H:>465==O E@OI>2>W B:0=8=8 01> AC3;>1V2, 0A>FV9>20=>3> 7 ;V:C20==OAC20==O F8?@>D;>:A0F8=C 70 V=H8<8 ?>:070==O<8, >:@V< ;V:C20==O ;535=528E CA:;04=5=L, A?@8G8=5=8E *Pseudomonas aeruginosa* C 4VB59 7 2VAF84>7< (2V:<>5-17 @>:V2), ;V:C20==O CA:;04=5=8E V=D5:FV9 A5G>282V4=8E H;OEV2 V ?VT;>=5D@8BC, A?@8G8=5=8E *E.coli* (2V:<>1-17 @>:V2), V A81V@AL:>W 28@07:8 ?VA;O :>=B0:BC =5 282G0;>AO. ;V=VG=89 4>A2V4 70AB>AC20==O F8?@>D;>:A0F8=C 4VBO< 70 V=H8<8 ?>:070==O<8 >1<565=89.

0AB>AC20==O F8?@>D;>:A0F8=C 4VBO< B0 ?V4;VB:0< A;V4 ?@>2>48B8 73V4=> 7 4VNG8<8 >DV9=8<8 @5:><5=40FVO<8. V:C20==O 7 70AB>AC20==O< F8?@>D;>:A0F8=C <0T ?@>2>48B8 ;8H5 ;V:0@ V7 4>A2V4< 2545==O 4VB59 B0 ?V4;VB:V2, E2>@8E =0 :VAB>7=89 DV1@>7 B0/01> BO6:V V=D5:FVW.

V428I5=0 GCB;82VABL 4> ?@5?0@0BC. # 450:8E 28?04:0E 3V?5@GCB;82VABL B0 0;5@3VG=V @50:FVW <>6CBL A?>AB5@V30B8AO 265 ?VA;O ?5@H>3> 70AB>AC20==O F8?@>D;>:A0F8=C, ?@> I> A;V4 =5309=> ?>2V4<>8B8 ;V:0@O.

?>>48=>:8E 28?04:0E 0=0DV;0:B8G=V/0=0DV;0:B>W4=V @50:FVW<>6CBL ?@>3@5AC20B8 4> AB0=C H>:C, I> 703@>6CT 68BBN ?0FVT=B0. # 450:8E 28?04:0E 2>=8 A?>AB5@V30NB8AO 265 ?VA;O ?5@H>3> 70AB>AC20==O F8?@>D;>:A0F8=C. # F8E 28?04:0E ?@89<< F8?@>D;>:A0F8=C =5>1EV4=> ?@87C?8=8B8 V =5309=> ?@>25AB8 <548:0<5=B>7=5 ;V:C20==O (;V:C20==O 0=0DV;0:B8G=>3> H>:C). (;C=:>2>-.8H:>289 B@0:B. # 28?04:C 28=8=:5==O ?@>BO3<< 01> ?VA;O ;V:C20==O BO6:>W V ABV9:>W 4V0@5W ?@> F5 A;V4 ?>2V4<>8B8 ;V:0@O, >A:V;L:8 F59 A8< <65 <0A:C20B8 BO6:5 H;C=:>2>-.8H:>25 70E2>@N20==O (=0?@8;;04, ?A524<<5<1@0=>7=89 :>;VB, I> <>65 703@>6C20B8 68BBN 7 <>6;828< ;5B0;L=8< =0A;V4:><), O:5 28<030T =5309=>3> ;V:C20==O. # B0:8E 28?04:0E ?@89<< F8?@>D;>:A0F8=C =5>1EV4=> ?@8?8=8B8 V @>7?>G0B8 70AB>AC20==O 2V4?>2V4=>W B5@0?VW (=0?@8;;04, 20=:>@0;L=> 4x250 <3/4>1C). V:0@AL:V 70A>18, O:V ?@83=VGCNBL ?5@8AB0;LB8:C, ?@>B8?>:070=V.

V4>< ?@> 28?04:8 0=B81V>B8:-0A>FV9>20=>W 4V0@5W, A?@8G8=5=>W *Clostridium Difficile* O:0
<65 20@VN20B8AO 2V4?>2V4=> 4> BO6:>ABV 2V4 ;53:>W 4V0@5W 4> ;5B0;L=>3> :>;VBC, ?@8
28:>@8AB0==V ?@0:B8G=> 2AVE 0=B810:B5@V0;L=8E ?@5?0@0BV2, C B>@8AB0==V
F8?@>D;>:A0F8=C. V:C20==O 0=B810:B5@V0;L=8<8 ?@5?0@0B0<8 A?@8G8=OT 7@<0;L=>W D;>@8
B>2AB>3> :8H5G=8:C, I>, C A2>N G5@3C, ?@872>48BL 4> =043> @>ABC *Clostridium Difficile*.
Clostridium Difficile?@>4C:CT B>:A8=8 V, O:V A?@8ONBL @>728B:C 0=B81V>B8:-0A>FV9>20=>W
4V0@5W. *Clostridium Difficile*?@>4C:CT 25;8:C :V;L:VABL B>:A8=C, A?@8G8=OT ?V428I5==O
70E2>@N20=>ABV B0 ;5B0;L=>ABV G5@57 <6;82C ABV9:VABL 71C4=8:0 4> 0=B8I=>W B5@0?VW
B0 =5>1EV4=VABL ?@>2545==O :>;5:B>1EV4=> ?0<OB0B8 ?@> <6;82VABL 28=8:=5==O 0=B81V>B8:-
0A>FV9>20=>W 4V0@5W, A?@8G8=5=>W *Clostridium Difficile* C 2AVE ?0FVT=BV2 7 4V0@5TN ?VA;O
70AB>AC20==O 0=B81V>B8:V2. 5>1EV4=89 @5B5;L=89 71V@ <548:0<5=B>7=>3> 0=0<=57C, >A:V;L:8
<6;8289 @>728B>: 0=B81V>B8:-0A>FV9>20=>W 4V0@5W, A?@8G8=5=>W *Clostridium Difficile*
?@>BO3>< 42>E 4V03=>7 0=B81V>B8:-0A>FV9>20=>W 4V0@5W, A?@8G8=5=>W *Clostridium Difficile*
@>73;O40TBLAO 01> 265 ?V4B25@465=89, 28:>@8AB0==O 0=B81V>B8:V2, O:V =5 4VNBL =0
Clostridium Difficile <6;82>, =5>1EV4=> 1C45 ?@8?8=8B8. 0;56=> 2V4 ;:V=VG=8E 40=8E =5>1EV4=>
?@>2>48B8 :>@5:FVN 2>4=>:5;5:B@>;VB=>3> 10;0=AC, @>73;O=CB8 =5>1EV4=VABL 4>40B:>2>3>
22545==O 1V;:>28E ?@5?0@0BV2, 70AB>AC20B8 0=B810:B5@V0;L=V ?@5?0@0B8, 4> O:8E T
GCB;82>N *Clostridium Difficile* "0:>6 <65 28=8:=CB8 =5>1EV4=VABL EV@C@3VG=>3> 2B@CG0==O.
@8 70AB>AC20==V F8?@>D;>:A0F8=C ?>2V4<<O;>AO ?@> 28?04:8 @>728B:C =5:@>7C ?5GV=:8 B0
?5GV=:>2>W =54>AB0B=>ABV 7 703@>7>N 68BBN ?0FVT=B0. # 28?04:C ?>O28 1C4L-O:8E >7=0: V A8
@N20==O ?5GV=:8 (B0:8E O: 0=>@5:AVO, 6>2BO=8FO, B5<=0 A5G0, A25@1V6 01> =0?@C65=VABL
?5@54=L>W G5@52=>W ABV=:8), ;V:C20==O A;V4 ?@8?8=8B8. "0:>6<65 287=0G0B8AO B825
71V;LH5==O @V2=O B@0=A0W D>AD0B878, @>728B>: E>;5AB0B8G=>W 6>2BO=8FV, >A>1;82> C
?0FVT=BV2 7 ?>?5@54=V< CH:>465==O< ?5GV=:8.
O7>2>-A:5;5B=0 A8AB5<0. □030;>< F8?@>D;>:A0F8= =5 <6=0 70AB>A>2C20B8 ?0FVT=B0< V7
70E2>@N20==O<8 ACE>68;L B0 @>7;040<8, ?>2O70=8<8 V7 70AB>AC20==O< EV=>;V=V2 2 0=0
<=57V. 572060NG8 =0 F5, C @V4:VA=8E 28?04:0E ?VA;O1V>;>3VG=>3> 4>A;V465==O 71C4=8:0 B0
>FV=:8 A?V22V4=>H5==O :>@8ABL/@878: F8< ?0FVT=B0< <65 1CB8 ?@87=0G5=89 F8?@>D;>:A0F8=
4;O ;V:C20==O >:@5<8E BO6:8E V=D5:FV9=8E ?@>F5AV2, 0 A0<5 - C 28?04:C =55D5:B82=>ABV
AB0=40@B=>W B5@0?VW 01> 10:B5@V0;L=>W @578AB5=B=>ABV, :>;8 @57C;LB0B81V>;>3VG=8E
4>A;V465=L 28?@024>2CNBL 70AB>AC20==O F8?@>D;>:A0F8=C. @8 70AB>AC20==V
F8?@>D;>:A0F8=C <65 28=8:=CB8 B5=48=VB 01> @>7@82 ACE>68;;O (>A>1;82> 0EV;;>2>3>
ACE>68;;O), V=>4V 42>1VG=89, C ?5@HV 48 3>48= ;V:C20==O. 878: B5=48=>?0BVW <65 1CB8
?V428I5=8< C ?0FVT=BV2 ;VB=L>3> 2V:C 01> C ?0FVT=BV2, O:V >4=>G0A=> ?@89<0NBL
:>@B8:>AB5@>W48 (482. @>74V; <<1VG=V @50:FVW»). @8 28=8:=5==V 1C4L-O:8E >7=0: B5=48=VBC
(=0?@8;;04, 1>;NG89 =01@O.; 70?0;5==O) 70AB>AC20==O F8?@>D;>:A0F8=C A;V4 ?@8?8=8B8.
#@065=V9 :V=FV2FV A;V4 70157?5G8B8 A?>:V9.
5@2>20 A8AB5<0. %2>@V =0 5?V;5?AVN V ?0FVT=B8, O:V<0NBL 2 0=0<=57V ?>@CH5==O DC=:FVW
F5=B@0;L=>W =5@2>2>W A8AB5<8 (=0?@8;;04, 7=865==O AC4<=>3> ?>@>3C, AC4<8 2 0=0<=57V, 7
<5=H5==O V=B5=A82=>ABV F5@51@0;L=>3> :@>2>>1V3C, 7;>2=>3> <7:C 01> V=AC;LB), <6CBL
?@89<0B8 F8?@>D;>:A0F8=, BV;L:8 O:I> >GV:C20=0 :>@8ABL ?5@52060T<6;8289 @878.; >A:V;L:8
B0:V E2>@V =0;560BL 4> 3@C?8 @878:C G5@57 <6;82V ?>1VG=V @50:FVW 7 1>:C F5=B@0;L=>W
=5@2>2>W A8AB5<8.
450:8E 28?04:0E ?>1VG=V @50:FVW 7 1>:C F5=B@0;L=>W =5@2>2>W A8AB5<8
A?>AB5@V30NBLAO 265 ?VA;O ?5@H>3> 70AB>AC20==O F8?@>D;>:A0F8=C. # ?>>48=>:8E 28?04:0E
45?@5AVO 01> ?A8E>7 <6CBL ?@>3@5AC20B8 4> AB0=C, I> 703@>6CT 68BBN ?0FVT=B0. # B0:8E
28?04:0E ?@89>< F8?@>D;>:A0F8=C =5>1EV4=> ?@8?8=8B8 V =5309=> ?>2V4<<8B8 ;V:0@O.
(:V@0 V?V4H:V@=0 ;:VB:>28=0. C;> 4>2545=>, I> F8?@>D;>:A0F8= A?@8G8=OT 28=8:=5==O
@50:FV9 D>B>GCB;82>ABV, B>B>GCB;82>ABV (?>4V1=8E 4> A>=OG=8E >?V:V2) B5@0?VN
F8?@>D;>:A0F8=>< A;V4 ?@8?8=8B8.
&8B>E@>< 450. □V4><, I> F8?@>D;>:A0F8= T V=3V1VB>@< ?>W 4VW D5@<5=BV2 12 F8B>E@>
B@815@56=>ABV ?@8 >4=>G0A=>AC20==V F8?@>D;>:A0F8=C V ?@5?0@0BV2, O:V
<5B01>;V7CNBLAO 0=0;>3VG=8< D5@<5=B=8< H;OE<< (B0:8E O: B5>DV;V=, <5B8;;A0=B8=, :>D5W=,
4C;>:A5B8=, ;:>70?V=). 1V;LH5==O :>=F5=B@0FVW F8E ?@5?0@0BV2 C A8@>20BFV :@>2V
?>2O70=5 7 ?@83=VG5==O< WE <5B01>;VG=>3> ;:V@5=AC F8?@>D;>:A0F8=><, I> <65 28;;8:0B8

A?5F8DVG=V ?>1VG=V 5D5:B8.
?:82 =0 @57C;LB0B8 ;01>@0B>@=8E 0=0;V7V2. ?>:A0F8= in vitro <>65 2?;820B8 =0 @57C;LB0B8
?>AV2C =0 Mycobacterium spp. H;OE<< ?@83=VG5==O @>ABC :C;LBC@8 10:B5@V9, I> <>65
?@8725AB8 4> ?A524>=530B82=8E @57C;LB0BV2 0=0;V7C ?>AV2C 2V4 ?0FVT=BV2, O:V ?@89<0NBL
F8?@>D;>:A0F8=
?>:A0F8= =5 A;V4 70AB>A>2C20B8 2 O:>ABV <>=>B5@0?VW 4;O ;V:C20==O BO6:8E V=D5:FV9,
28;;8:0=8E 3@078B82=8<8 01> 0=05@>1=8<8 10:B5@VO<8.
V0@5O <0=4@V2=8:0.
@8 281>@V F8?@>D;>:A0F8=C A;V4 27OB8 4> C2038 V=D>@<0FVN ?@> @578AB5=B=VABL 4>
F8?@>D;>:A0F8=C 2V4?>2V4=8E >@30=V7
=D5:FVW :VAB>: B0 AC3;>1V2.
?>:A0F8= A;V4 70AB>A>2C20B8 C :<<1V=0FVW 7 V=H8<8 0=B81=8<8 70A>10<8 70;56=> 2V4
@57C;LB0BV2 1V>;>3VG=>3> 4>A;V465==O.

535=520 D>@<0 A81V@AL:>W 28@07:8.
0AB>AC20==O ;N4O< 70A=>20=5 =0 40=8E 287=0G5==O GCB;82>ABV in-vitro, 4>A;V4V2 =0
B20@8=0E @07>< V7 >1<565=8<8 40=8<8, >B@8<0=8<8 C ;N459. V:0@ ?>28=5= 4VOB8 2V4?>2V4=> 4>
=0FV>=0;L=8E B0/01> 4=8E ?@>B>:>;V2 ;V:C20==O A81V@AL:>W 28@07:8.
?>:A0F8= 70AB>A>2C20B8 7 >15@56=VABN ?0FVT=B0< V7
4=>G0A=5 ?@87=0G5==O F8?@>D;>:A0F8=C V <5B>B@5:A0BC =5 @5:><5=4CTBLAO.
@>=E>-,535=52V V=D5:FVW ?@8 :VAB>7=>7V. ;V=VG=V 28?@>1C20==O 2;;NG0;8 4VB59 B0
?V4;VB:V2 2V:< 5-17 @>:V2. V;LH >1<565=89 4>A2V4 VA=CT C ;V:C20==V 4VB59 2V:< 2V4 1 4>
5 @>:V2.
#A:;04=5=V V=D5:FVW A5G>2>3> B@0:BC B0 ?VT;>=5D@8B. !;V4 @>73;O=CB8 <>6;82VABL
;V:C20==O V=D5:FV9 A5G>2>3> B@0:BC 7 70AB>AC20==O< F8?@>D;>:A0F8=C, :>;8 V=H5 ;V:C20==O
=5<>6;825. V:C20==O<0T '@C=BC20B8AO =0 @57C;LB0B0E 1V>;>3VG=>3> 4>A;V465==O.
8@.:8 B0 A5G>284V;L=0 A8AB5<0. >2V4><;O;>AO ?@> :@8AB0;C@VN, ?>2O70=C 7 70AB>AC20==O<
F8?@>D;>:A0F8=C. 0FVT=B8, O:V ?@89<0NBL F8?@>D;>:A0F8=, ?>28==V >B@8AB0B=N ;V;L:VABL
@V48=8. !;V4 C=8:0B8 =04W ;C6=>ABV A5GV.
578AB5=B=VABL. V4 G0A 01> ?VA;O :C@AC ;V:C20==O F8?@>D;>:A0F8=× @578AB5=B=V
10:B5@VW <>6CBL 1CB8 284V;5=V 7 01> 157 ;;V=VG=> 287=0G5=>W AC?5@V=D5:FVW. >65
VA=C20B8 ?52=89 @878: 284V;5==O F8?@>D;>:A0F8=-@578AB5=B=8E 10:B5@V9 ?V4 G0A B@820;8E
:C@AV2 ;V:C20==O B0 ?@8 ;V:C20==V 2=CB@VH=L>;V:0@=O=8E V=D5:FV9 B0/01> V=D5:FV9,
A?@8G8=5=8E 2840<8 Staphylococcus V Pseudomonas.

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<0<8.
02VBL :>;8 ?@5?0@0B ?@89<0B8 B>G=> 70 2:07V2:0<8 ;V:0@O, 2V= <>65 2?;820B8 =0 H284:VABL
@50:FVW, I> <>65 ?5@5H:>460B8 :5@C20==N 02B><>1V;5< 01> @>1>BV 7 V=H8<8 <5E0=V7<0<8. &5
>A>1;82> E0@0:B5@=> ?@8 70AB>AC20==V ?@5?0@0BC ?0@0;5;L=> 7 0;>3>;5

70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9.
!;V4 4>B@815@56=>ABV ?@8 >4=>G0A=>AC20==V F8?@>D;>:A0F8=C B0 0=B80@8B ,
B@8F8;;VG=8E 0=B845?@5A0=BV2, <0:@>;V4V2, 0=B8?A8E>B8:V2, >A:V;L:8 F8?@>D;>:A0F8= <0T
048B82=89 5D5:B ?@8 ?>4>265==V V=B5@20;C QT (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).
\$>@3> :>@8 >4=>G0A=>AC20==V F8?@>D;>:A0F8=C (?5@>@0;L=>) B0 ;V:0@AL:8E 70A>1V2, I>
20;5=B=V :0BV=>8, 102>: (=0?@8:;04 :0;LFFVN, <03=VN, 0;NAD0B72'O7CNG8E ?>;V<5@V2 (=0?@8:;04,
A525;0<5@, ;0=B0=C :0@1>=0B), AC:@0;LD0BV2 01> 0=B0F84V2, 0 B0:>6 V7 ?@5?0@0B0<8 7 25;8:>N
1CD5@=>N T<=VABN (=0?@8:;04, B01;5B:8 4840=>78=C), I> :0;LFFV9, 01A>@1FVO F8?@>D;>:A0F8=C
7=86CTBLAO. # 72O7:C 7 F8< F8?@>D;>:A0F8= A;V4 ?@89<0B8 01> 70 1-2 3>48=8 4> 01> G5@57 4
3>48=8 ?VA;O ?@89>
0=5 >1<565==O =5 AB>ACTBLAO 0=B0F84V2, I> =0;560BL 4> ::0AC 1;>:0B>@V2 H2-@5F5?B>@V2.

>;>G=V B0 V=HV E0@G>2V ?@>4C:B8. !;V4 C=8:0B8 >4=>G0A=>3> 70AB>AC20==O
F8?@>D;>:A0F8=C V <>;>G=8E 01> 71030G5=8E < :0;LFDVN). 5HB0 ?@>4C:BV2 7 2< :0;LFDVN 7=0G=>N
N =5 2?;820NBL =0 2A<>:BC20==O F8?@>D;>:A0F8=C.
@>15=5F84. @>15=5F84 A?>2V;L=NT 282545==O F8?@>D;>:A0F8=C 7 6>2GN. 4=>G0A=5
70AB>AC20==O ;V:0@AL:8E 70A>1V2, I> 15=5F84 B0 F8?@>D;>:A0F8=C, ?@872>48BL 4> ?V428I5==O
:=F5=B@0FVW F8?@>D;>:A0F8=C C ?;072V. @>15=5F84 2?;820T =0 =8@>:2C A5:@5FVN
F8?@>D;>:A0F8=C.
5B>;>?@05B>;>?@0@NT 2A<>:BC20==O F8?@>D;>:A0F8=C (?@8 ?5@>@0;L=> ?@872>48BL 4>
A:>@>G5==O G0AC 4> 4>AO3=5==O <0:A8<0;L=>W :=F5=B@0FVW ?@5?0@0BC C ?;072V. 0
1V>4>ABC?=VABL F8?@>D;>:A0F8=C 6>4=>3> 2?;82C =5 A?>AB5@V30;>AO.
<5?@07>;. 4=>G0A=5 70AB>AC20==O F8?@>D;>:A0F8=C B0 ;V:0@AL:8E 70A>1V2, I> <5?@07>;,
?@872>48BL 4> =57=0G=>3> 7=865==O C_{max} V ?>:07=8:0 «?;>I0 ?V4 :@82>N A?V22V4=>H5==O
:=F5=B@0FVO-G0A (AUC)» F8?@>D;>:A0F8=C.
"870=V48=. V 71V;LH5==O< :=F5=B@0FVW B870=V48=C 2 A8@>20BFV :@>2V 0A>FVNNBLAO
3V?>B5=782=V B0 A540B82=V ?>1VG=V @50:FVW. "4=>G0A=5 70AB>AC20==O F8?@>D;>:A0F8=C V
;V:0@AL:8E 70A>1V2, I> B8?>:070=5 (482. @>74V; «@>B8?>:070==O»).

"5>DV;V=. 4=>G0A=5 70AB>AC20==O F8?@>D;>:A0F8=C B0 ;V:0@AL:8E 70A>1V2, I> DV;V=, <>65
?@8725AB8 4> =51060=>3> ?V428I5==O :=F5=B@0FVW B5>DV;V=C C ?;072V, I> <>65 A?@8G8=8B8
@>728B>: ?>1VG=8E @50:FV9. # ?>>48=>:8E 28?04:0E B0:V ?>1VG=V @50:FVW <>6CBL
703@>6C20B8 68BBN 01> <0B8 ;5B0;L=89 =0A;V4>:./:I> >4=>G0A=>3> 70AB>AC20==O F8E
?@5?0@0BV2 C=8:=CB8 =5 <>6=0, A;V4 :=B@>;N20B8 :=F5=B@0FVN B5>DV;V=C 2 A8@>20BFV
:@>2V B0 045:20B=> 7=86C20B8 9>3> 4>7C (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

=HV ?>EV4=V :A0=B8=C. VA;O >4=>G0A=>3> 70AB>AC20==O F8?@>D;>:A0F8=C B0 70A>1V2, I>
D5W= 01> ?5=B>:A8DV;V= (>:A?5=B8DV;V=), ?>2V4<;O;>AO ?@> ?V428I5==O :=F5=B@0FVW F8E
:A0=B8=V2 C A8@>20BFV :@>2V.

5B>B@5:A0B. @8 >4=>G0A=>D;>:A0F8=C <>6;825 C?>2V;L=5==O BC1C;O@=>3> B@0=A?>@BC20==O
(=8@>:289 <5B01>;V7<) <5B>B@5:A0BC, I> <>65 ?@872>48B8 4> ?V428I5==O :=F5=B@0FVW
<5B>B@5:A0BC C ?;072V. @8 FL>G0A=5 ?@87=0G5==O F8?@>D;>:A0F8=C V <5B>B@5:A0BC =5 @5:>
<5=4CTBLAO.

5AB5@>W4=V ?@>B870?0;L=V 70A>18. >A;V465==O =0 B20@8=0E ?>:070;8, I> :<>1V=>20=5
70AB>AC20==O 4C65 28A>:8E 4>7 EV=>;>=V2 (V=3V1VB>@V2 3V@078) V 450:8E =5AB5@>W4=8E
?@>B870?0;L=8E ?@5?0@0BV2 (>:@V< 0F5B8;A0;VF8;>2>W :8A;>B8) <>65 ?@>2>:C20B8 AC4<8.
?>A?>@8=. @8 >4=>G0A=>AC20==V F8?@>D;>:A0F8=C B0 F8;>A?>@8=C A?>AB5@V30;>AO
B@0=78B>@=5 ?V428I5==O :=F5=B@0FVW A8@>20B:>2>3> :@50B8=V=C. ">
=B03>=VAB8 2VB0@8 >4=>G0A=>AC20==V F8?@>D;>:A0F8=C B0 0=B03>=VAB0 2VB0G=> >FV=8B8
2?;82 F8?@>D;>:A0F8=C =0 ?V428I5==O 7=0G5==O V6=0@>4=>3> =>@<0;V7>20=>3> 2V4=>H5==O ()
A:;04=>. !;V4 74V9A=N20B8 G0AB89 :=B@>;L ?V4 G0A V >4@07C ?VA;O >4=>G0A=>3> 22545==O
F8?@>D;>:A0F8=C B0 0=B03>=VAB0 2VB0:C<0@>;C, D5=?@>:C<>=C 01> D;CW=4V=>C). A=CNBL
?>2V4<>;5==O ?@> ?V428I5==O 0:B82=>ABV >@0;L=8E 0=B8:>03C;O=BV2 C ?0FVT=BV2, O:V >B@8
:@5<0 DB>@EV=>;>=8.
C;>:A5B8=. 572060NG8 =0 2V4ACB=VABL ;V=VG=8E 40=8E, <>6=0 ?5@5410G8B8 <>6;82VABL 270T
<>4VW ?@8 >4=>G0A=>AC20==V F8?@>D;>:A0F8=C B0 4C;>:A5B8=C (482. @>74V; «A>1;82>ABV
70AB>AC20==O»).

>?V=V@>;. >=VB>@8=3 ?>1VG=8E 5D5:BV2 @>?V=V@>;C B0 2V4?>2V4=5 :=@53C20==O 4>78 @5:>
<5=4CTBLAO 74V9A=N20B8 ?V4 G0A V >4@07C ?VA;O AC3> 22545==O 7 F8?@>D;>:A0F8=C< (482.
@>74V; «A>1;82>ABV 70AB>AC20==O»).

V4>:0W=. >A;V465==O 7 CG0ABN 74>@>28E 4>1@>2>;LFDV2 ?>:070;8, I> >4=>G0A=5 70AB>AC20==O
;V:0@AL:8E 70A>1V2, I> :0W= B0 F8?@>D;>:A0F8=C, V=3V1VB>@ V7>5=78W 4VW, ?@872>48BL 4> 7
<5=H5==O ;V@5=AC ;V4>:0W=C, O:89 1C2 22545=89 2=CB@VH=L>25==>, =0 22 %. %>G0 ;V4>:0W=
4>1@5 ?5@5=>A8BLAO, ?VA;O >4=>G0A=>3> 70AB>AC20==O 9>3> 7 F8?@>D;>:A0F8=C< <>65
A?>AB5@V30B8AO ?52=0 270T<>4VO, O:0 <>65 AC?@>2>46C20B8AO ?>1VG=8<8 @50:FVO<8.
>70?V=. VA;O >4=>G0A=>3> 70AB>AC20==O 250<3 F8?@>D;>:A0F8=C 7 ;>70?V=<< C?@>4>26

7 4=V2 A8@>20B:>2V :=F5=B@0FVW ;;>70?V=C V N-45A<5B8;;;>70?V=C 1C;8 ?V428I5=V =0 29 % V
31 % 2V4?>2V4=>. ;V=VG=89 =03;04 B0 2V4?>2V4=C :>@5:FVN 4>78 ;;>70?V=C @5:><5=4CTBLAO
74V9A=N20B8 ?V4 G0A V >4@07C ?VA;O >4=>G0A=>3> 70AB>AC20==O 7 F8?@>D;:>.A0F8=< (482.
@>74V; «A>1;82>ABV 70AB>AC20==O»).

!8;45=0DV; V4 G0A 4>A;V465=L 7 CG0ABN 74>@>28E 4>1@>2>;LFV2 1C;> 28O2;5=>, I> C_{max} B0 AUC
A8;45=0DV;C ?V428ICNBLAO ?@81;87=> 242VGV ?VA;O ?5@>@0;L=>3> 70AB>AC20==O 50<3
>4=>G0A=> 7 500 <3 F8?@>D;:>.A0F8=C. !;V4 7 >15@56=VABN ?@87=0G0B8 F8?@>D;:>.A0F8=
>4=>G0A=> V7 A8;45=0DV;<, @5B5;L=> >FV=NNG8 A?V22V4=>H5==O «@878:->@8ABL».

§5=VB>W=. 4=>G0A=5 ?@87=0G5==O F8?@>D;:>.A0F8=C B0 D5=VB>W=C <>65 ?@8725AB8 4>
?V428I5==O 01> 7=865==O A8@>20B:>28E :=F5=B@0FV9 D5=VB>W=C, B<5=4CTBLAO
<>=VB>@8=3 @V2=V2 ?@5?0@0BC.

5@>@0;L=V FC:@>7=86C20;L=V 70A>I8. @8 AC?CB=L>@0;L=8E 0=B84V015B8G=8E ?@5?0@0BV2,
>A>1;82> 3@C?8 AC;LD=>V;A5G>28=8 (=0?@8;:04, 3;V15=:;0?>2O70=0, 2V@>3V4=>, 7
?>B5=FVN20==O< F8?@>D;:>.A0F8=<< 4VW ?5@>@0;L=8E 0=B84V015B8G=8E 70A>1V2 (482. @>74V;
<>1VG=V @50:FVW»).

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

\$0@<0:>48=0

5E0=V7< 4VW. ?>.A0F8= in vitro 28O2;OT 28A>.C 5D5:B82=VABL I>4> H8@>:>3> A?5:B@0 3@0
<=530B82=8E V 3@078B82=8E 71C4=8:V2. 5E0=V7< 0=B810:B5@V0;L=>W 4VW >1C<>2;5=89
740B=VABN F8?@>D;:>.A0F8=C ?@83=VGC20B8 B?>V7<5@078 B8?C (-3V@07C B0 B?>V7<5@07C
IV), O:V T =5>1EV4=8<8 C 1030BL>E ?@>F5A0E 68BBT2>3> F8;:C , B0:8E O: @5?;V:0FVO,
B@0=A:@8?FVO, @5?0@0FVO V @5:<1V=0FVO.

5E0=V7< @578AB5=B=>ABV. 578AB5=B=VABL 4> F8?@>D;:>.A0F8=C Vn vitro 70728G09 ?>2O70=0 7
?>V7<5@070E V -3V@07V H;OE< 1030B>ABC?5=528E F8?@>D;:>.A0F8=C B0 ?5@5E@5A=C
@578AB5=B=VABL 4> EV=>;>=V2.

5E0=V7<8 @578AB5=B=>ABV, O:V V=0:B82CNBL V=HV 0=B81V>B8:8, B0:V O: 7=865==O
?@>=8:=>ABV 7>2=VH=L>W ABV=:8 10:B5@VW (?@8B0<0==> 4;O *Pseudomonas aeruginosa*) B0
0:B82=5 282545==O ?@5?0@0BC 7 ;:VB8=8 (5D;N:A), <>6CBL 2?;8=CB8 =0 GCB;82VABL 4>
F8?@>D;:>.A0F8=C. >2V4<<;O;>AO ?@> @>728B>: ?;07?>A5@54:>20=>W @578AB5=B=>ABV,
:>4>20=>W qnr 35=<< 0=B81V>B8:>@578AB5=B=>ABV. 5E0=V7<8 @578AB5=B=>ABV, O:8<8
V=0:B82CNBLAO ?5=VF8;V=8, F5D0;>A?>@8=8, 03;V:>7848, <0:@>;V48 V B5B@0F8;V=8, <>6CBL =5
2?;820B8 =0 0=B810:B5@V0;L=C 0:B82=VABL F8?@>D;:>.A0F8=C. @30=V7<8, ABV9:V 4> F8E
?@5?0@0BV2, <>6CBL 1CB8 GCB;828<8 4> F8?@>D;:>.A0F8=C.

V=V<0;L=0 10:B5@8F84=0 :=F5=B@0FVO (M), O: ?@028;>, =5 ?5@528ICT

'CB;82VABL 4> F8?@>D;:>.A0F8=C Vn vitro.>H8@5=VABL =01CB>W @578AB5=B=>ABV 284V;5=8E
284V2 <>65 20@VN20B8 70;56=> 2V4 ABV V G0AC, B>1EV4=0 ;>:0;L=0 V=D>@<0FVO ?@>
@578AB5=B=VABL, >A>1;82> ?@8 ;V:C20==V BO6:8E V=D5:FV9. @8 =5>1EV4=>ABV A;V4
725@=CB8AO 70 :=AC;LB0FVTN 4> A?5FV0;VABV2, :>;8H8@5=VABL @578AB5=B=>ABV =01C;0
B0:>3> @V2=O, I> :>@8ABL 2V4 70AB>AC20==O 70A>1C I>4> 45O:8E 284V2 V=D5:FV9 T AC
<=V2=>N.

> F8?@>D;:>.A0F8=C 7030;>< GCB;82V in vitro=0ABC?=V @>48 B0 2848 10:B5@V9:

05@>I=V 3@078B82=V>@30=V7<8 (*Bacillus anthracis*, *Staphylococcus aureus*, *Staphylococcus*
saprophyticus, *Streptococcus* spp.);

05@>I=V 3@0<=530B82=V>@30=V7<8 (*Aeromonas* spp., *Brucella* spp., *Citrobacter koseri*, *Francisella*
tularensis, *Haemophilus ducreyi*, *Haemophilus influenzae*, *Legionella* spp., *Moraxella catarrhalis*, *Neisseria*
meningitidis, *Pasteurella* spp., *Salmonella* spp., *Shigella* spp. *Vibriosp.* *Yersinia pestis*);

0=05@>I=V>@30=V7<8 (*Mobiluncus*);

V=HV >@30=V7<8: (*Chlamydia trachomatis*, *Chlamydia pneumoniae*, *Mycoplasma hominis*, *Mycoplasma*
pneumoniae).

V7=C GCB;82VABL 4> F8?@>D;:>.A0F8=C 28O2;ONBL:*Acinetobacter baumann*, *Burkholderia cepacia*,
Campylobacter spp., *Citrobacter freundii*, *Enterococcus faecalis*, *Enterobacter aerogenes*, *Enterobacter cloacae*,
Escherichia coli, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Morganella morganii*, *Neisseria gonorrhoeae*, *Proteus*
mirabilis, *Proteus vulgaris*, *Providenciaspp.*, *Pseudomonas aeruginosa*, *Pseudomonas fluorescens*, *Serratia*
marcescens, *Streptococcus pneumoniae*, *Peptostreptococcus* spp., *Propionibacterium acnes*

2060TBLAO, I> =0ABC?=V >@30=V7<8 28O2;ONBL A?04:>2C @578AB5=B=VABL 4>
F8?@>D;>:A0F8=C: *Staphylococcus aureus* (<5B8F8;V=@578AB5=B=V) B0 *Stenotrophomonas maltophilia*,
Actinomyces, *Enterococcus faecium*, *Listeria monocytogenes*, *Mycoplasma genitalium*, *Ureaplasma urealitycum*,
0=05@>1=V >@30=V7<8 (70 28=OB:>< *Mobiluncus*, *Peptostreptococcus*, *Propionibacterium acnè*;
0=V I>4> ;535=52>W D>@<8 A81V@AL:>W 28@07:8
5:><5=40FVW I>4> 70AB>AC20==O ;N48=V 107CNBLAO 2 >A=>2=>ABV >@30=V7 *in vitro*, =0 40=8E
4>A;V465=L =0 5:A?5@8<5=B0;L=8E B20@8=0E B0 =0 >1<565=8E 40=8E I>4> 70AB>AC20==O ;N48=V.
D5:B82=8< 22060TBLAO 70AB>AC20==O F8?@>D;>:A0F8=C ?@>B03>< 42>E 7V 500 <3 4;O
70?>1V30==O 70E2>@N20==O =0 A81V@AL:C 28@07:C C ;N48=8. V:0@ ?>28=5= ?@>2>48B8
;V:C20==O 73V4=> 7 =0FV>=0;L=8<8 B0/01> 4=8<8 :>=A5=AC0;L=8<8 4>;C<5=B0<8 I>4> ;V:C20==O
A81V@AL:>W 28@07:8.
\$0@<0:>:V=5B8:0.
\$0@<0:>:V=5B8:0 F8?@>D;>:A0F8=C 282G0;0AL C @V7=8E ;N4AL:8E ?>?C;OFVOE. >ABV9=0 A
5@54=O ?V:>20 :>=F5=B@0FVO F8?@>D;>:A0F8=C C A8@>20BFV 4>@>A;8E >AV1, O:V ?@>89<0;8 ?>
500 <3 ?5@>@0;L=> :>6=V 12 3>48=, AB0=>28BL 2,97
IA>@IFVO. VA;O ?5@>@0;L=>3> 70AB>AC20==O B01;5B>: F8?@>D;>:A0F8=C C 4>7V 250 <3 B0
500 <3 F8?@>D;>:A0F8= H284:> B0 4>1@5 2A<>:BCTBLAO, ?5@5206=> 7 25@E=L>3> 2V44V;C
B>=>3> :8H5G=8:C.
0:A8<0;L=V :>=F5=B@0FVW C A8@>20BFV :@>2V 4>AO30NBLAO G5@57 1-2 3>48=8.
1A>;NB=0 1V>4>ABC?=VABL ?@5?0@0BC AB0=>28BL 70-80 %. 0:A8<0;L=V :>=F5=B@0FVW C
A8@>20BFV :@>2V (C_{max}) V 7030;L=0 ?;>I0 ?V4 :@82>N «:>=F5=B@0FVO/G0A» (AUC) ?V428IC20;8AO
7V 71V;LH5==O< 4>78.
>7?>4V;. V4A>B>: 72'07C20==O F8?@>D;>:A0F8=C 7 1V;:0<8 T =57=0G=8< (20-30 %), 2V=
7=0E>48BLAO C ?;072V ?5@5206=> 2 =5V>=V7>20=V9 D>@D;>:A0F8= 2V;L=> 48DC=4CT C
?>70AC48==89 ?@>ABV@. =0G=89 >1T< @>7?>4V;C C AB0=V ABV9:>W @V2=>2038, O:89
AB0=>28BL 2-3 ;/:3<0A8 BV;0, 4>2>48BL, I> F8?@>D;>:A0F8= ?@>=8:0T C B:0=8=8 C
:>=F5=B@0FVOE, O:V <>6CBL C 1030B> @07V2 ?5@528IC20B8 @V25=L ?@5?0@0BC 2 A8@>20BFV
:@>2V.
5B01>;V7C;8 70DV:A>20=V =528A>:V :>=F5=B@0FVW =0ABC?=8E G>B8@L>E<5B01>;VBV2:
4V5B8;F8?@>D;>:A0F8=C (1), AC;LD>F8?@>D;>:A0F8=C (2), >:A>F8?@>D;>:A0F8=C (3) B0 D>@
D;>:A0F8=C (4). 5B01>;VB8 1-3 28O2;ONBL *in vitro* 0=B81=C 0:B82=VABL, ?>4V1=C 01> =86GC 70
0:B82=VABL =0;V48:A>2>W :8A;>B8. 4 C =09<5=HV9 :V;L:>ABV T 5:2V20;5=B< =>@D;>:A0F8=C C
?;0=V 0=B81=>W 0:B82=>ABV *in vitro*.
82545==O. ?>:A0F8= 284V;OTBLAO 7451V;LH>3> C =57
VB8. V4?>2V4=> 4> 3@C?8 ?0FVT=BV2 B0 D0@<0:>:V=5B8G=>3> 0=0;V7C ?54V0B@8G=8E E2>@8E 7
@V7=8<8 V=D5:FVO<8, ?@>3=>7>20=89 A5@54=V9 ?5@V>4 =0?V2282545==O C 4VB59 AB0=>28BL
?@81;87=> 4-5 3>48=.

\$0@<0F52B8G=V E0@0:B5@8AB8:8.

A=>2=V DV78:>-EVABV:

B01;5B:8 :@C3;>W D>@<8, 2:@8BV >1>;>=:>N, 1V;>3> 01> 1V;>3> 7 6>2BC20B8< 2V4BV=:<< :>;L>@C,
25@E=O B0 =86=O ?>25@E=O O:8E >?C;>V. 0 @>7;073;O40==V ?V4 ;C?>N 284=> O4@>, >B>G5=5 >4=8
< ACFV;L=8< H0@>

"5@ABV.3 @>:8.

#<>28 715@V30==O.

15@V30B8 2 >@83V=0;L=V9 C?0:>2FV ?@8 B5>!.
15@V30B8 C =54>ABC?=>

#?0:>2:0.

"01;5B:8, 2:@8BV >1>;>=:>N, ?> 250 <3.

> 10 B01;5B>: C 1;VAB5@V; ?> 1 1;VAB5@C C ?0GFV 7 :0@B>=C;
?> 10 B01;5B>: C 1;VAB5@V; ?> 90 1;VAB5@V2 C :>@>1FV 7 :0@B>=C

"01;5B:8, 2:@8BV >1>;>=:>N, ?> 500 <3.

> 10 B01;5B>: C 1;VAB5@V; ?> 1 1;VAB5@C C ?0GFV V7 :0@B>=C;

?> 10 B01;5B>: C 1;VAB5@V; ?> 70 1;VAB5@V2 C :>@>1FV 7 :0@B>=C.

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

8@>1=8:.

@ " «"5E=>;>3».

VAF57=0E>465==O.

20300, #: @0W=0,