

!" #&/

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

"!□

("!□)

!;04:

4VNGV @5G>28=8: B>1@01 3 <07V 1@0

4>?>28=8: E;>@1CB0=>; 1572>4=89, >;VO .

V:0@AL:0 D>@<0. 07L >G=0.

A=>2=V DV78:>-EVABV: >4=>@V4=0 <07L 2V4 1V;>3> 4><0965 1V;>3> :>;L>@C.

\$0@<0:>B5@0?52B8G=0 3@C?0. @>B870?0;L=V B0 ?@>B81=V 70A>18 C :><1V=0FVW.

>@B8:>AB5@>W48 B0 ?@>B81=V 70A>18 C :><1V=0FVW. >4 "% S01C A01.

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

\$0@<0:>48=0

5:A0<5B07>=

D5:B82=VABL :>@B8:>AB5@>W4V2 4;O ;V:C20==O ?@>B870?0;L=8E AB0=V2 >:0 4>1@5 2V4×0.

>@B8:>AB5@>W48 4>AO30NBL A2>TW ?@>B870?0;L=>W 4VW H;OE× ?@83=VG5==O 04357VW

<>;5:C; 4> 5=4>B5;V0;L=8E ;;VB8= AC48=, F8;:>:A835=078 01> , B0 284V;5==O F8B>:V=V2. #

@57C;LB0BV FL>3> 7<5=HCTBLAO CB2>@5==O <54V0B>@V2 70?0;5==O B0 ?@83=VGCTBLAO

04357VO F8@:C;NNG8E ;59:>F8BV2 4> AC48==>3> 5=4>B5;VN, I> 70?>1V30T WE ?@>=8:=5==N C

70?0;5=V B:0=8=8 >:0. 5:A0<5B07>= G8=8BL 28@065=C ?@>B870?0;L=C 4VN 7V 7<5=H5=>N

:>@B8:>W4=>N 0:B82=VABN ?>@V2=O=> 7 45O:8<8 V=H8<8 AB5@>W40<8 B0 T >4=8< 7 =091V;LH

A8;L=>4VNG8E ?@>B870?0;L=8E 70A>1V2.

">1@0

">1@0:>0:B82=89 H284:>4VNG89 10:B5@8F84=89 0=B81V>B8: 3@C?8 03;V:>784V2, I> ?@>B84VT O:

3@078B82=8<, B0: V 3@0<=530B82=8< >@30=V7<03> <5E0=V7< 4VW ?>2O70=89 V7 ?@83=VG5==O<

:>;V?5?B84V2 B0 A8=B57C C @81>A×0E 10:B5@V0;L=8E ;;VB8=.

030;>< 4VO B>1@0?8A0=0 in vitroH;OE×< 287=0G5==O 0:B82=VABL 0=B81V>B8:0 ?@>B8 :>6=>3>

284C 10:B5@V9. A:V;L:8 B>1@0B8 1V;LH>ABV >G=8E ?0B>35==8E >@30=V7 2V= 22060TBLAO

0=B81V>B8:>< H8@>:>3> A?5:B@0 4VW. C:8 287=0G5=V :@8B8G=V 7=0G5==O , I> 287=0G0NBL

GCB;82VABL 01> @578AB5=B=VABL 10:B5@V0;L=>W :C;LBC@8 4> ?52=>3> 0=B81V>B8:0. A=CNG5

:@8B8G=5 7=0G5==O 4;O B>1@04> 2V4?>2V4=8E 284V2 10:B5@V9 2@0E>2CT 2;0AB82C

GCB;82VABL 284V2, 0 B0:>6<0:A8<0;L=C :>=F5=B@0FVN B0 D0@<0:>:V=5B8G=V 7=0G5==O

70;56=>ABV G0A/:>=F5=B@0FVO, 2820BFV :@>2V ?VA;O ?5@>@0;L=>3> 70AB>AC20==O.

87=0G5==O F8E :@8B8G=8E 7=0G5=L, I> ?>4V;OT>@30=V7<8 =0 GCB;82V B0 @578AB5=B=V,

28:>@8AB>2C20;8AL 4;O 287=0G5==O ;;V=VG=>W 5D5:B82=>ABV 0=B81V>B8:V2, I>

70AB>A>2C20;8AO A8AB5<=>. 4=0: ?@8 AC20==V 0=B81V>B8:0 C 28A>:8E :>=F5=B@0FVOE

157?>A5@54=L> =0 ?@>2>48;8AL. V;LHVABL>@30=V7AC20==V, =0A?@024V 4>1@5 @503CNBL =0

>@30=V7

V4 G0A ;;V=VG=8E 4>A;V465=L @>7G8= B>1@0 70AB>A>2C202AO , 28O282AO 5D5:B82=8< ?@>B8

1030BL>E VA=CNG8E HB035==8E 4;O >G59 >@30=V7A;V465==OE. 2060TBLAO, I> 45O:V 7 F8E

?0B>35==8E 4;O >G59 >@30=V7AC20==V. V4 G0A ;;V=VG=8E 4>A;V465=L 1C;> ?@>45>=AB@>20=>, I>

I> B>1@0 ?0B>35==88 >@30=V7<0<8.

@078B82=V 10:B5@VW:

Staphylococcus aureus (GCB;82V 4> <5B8F8;V=C 01> @578AB5=B=V*)

Staphylococcus epidermidis(GCB;82V 4> <5B8F8;V=C 01> @578AB5=B=V*)

=HV :>03C;07>=530B82=V 2848 *Staphylococcus*

*Streptococcus pneumoniae*5(GCB;82V 4> ?5=VF8;V=C 01> @578AB5=B=V*)

=HV 2848 *Streptococcus*.

* \$5=>B8? @578AB5=B=>ABV 15B0-;0:B01B> <5B8F8;V=C, ?5=VF8;V=C) =5 ?>2O70=89 V7 D5=>B8?<@578AB5=B=>ABV 03;V:>784V2 B0 >18420 =5 ?>2O70=V 7 2V@C;5=B=VABN B0 D5=>B8?0<8 ?0B>35==8E >@30=V7, I> 1030B> AB0DV;>:>V2, ABV9:8E 4><5B8F8;V=C, T ABV9:8<8 4> B>1@0 V=H8E 03;V:>784=8E 0=B81V>B8:V2). 4=0: FV ABV9:V AB0DV;>:>2V :C;LBC@8 (O: 287=0G5=> :@8B8G=8<8 7=0G5==O<8) 70728G09 4>1@5 @503CNBL =0 ;V:C20==O B>1@0<, I> 70AB>A>2CTBLAO .

□@0<=530B82=V 10:B5@VW:

Acinetobacter spp.

Citrobacter spp.

Enterobacter spp.

Escherichia coli

Haemophilus influenzae

Klebsiella pneumoniae

Moraxella spp.

Morganella morganii

Proteus mirabilis

Pseudomonas aeruginosa

Serratia marcescens.

>A;V465==O GCB;82>ABV 10:B5@V9 ?@>45<=>AB@C20;8, I> C 45O:8E 28?04:0E >@30=V7<8, ABV9:V 4> 35=B0W G0AB8=8 D;>@8 @578AB5=B=VABL 4> B>1@0728=C;0AO, >4=0: 10:B5@V0;L=0 @578AB5=B=VABL <65 @>728=CB8AO ?V4 G0A B@820;>3> 70AB>AC20==O.

>6;825 28=8:=5==O ?5@5E@5A=>W GCB;82>ABV 4> V=H8E 0=B81V>B8:V2 3@C?8 03;V:>784V2; C @07V 28=8:=5==O ?V428I5=>W GCB;82>ABV ?@8 70AB>AC20==V ?@5?0@0BC A;V4 ?@8?8=8B8 9>3> 70AB>AC20==O B0 ?@>25AB8 2V4?>2V4=5 ;V:C20==O.

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

5:A0<5B07>=

;V=VG=V D0@<0:>:V=5B8G=V 4>A;V465==O >G=>W <07V "!"® =5 ?@>2>48;8AO. 4=0: 4>A;V465==O, ?@>2545=V 7 >G=8<8 :@0?;O<8 "!"®, ?>:070;8, I> A8AB5<=89 2?;82 45:A0<5B07>=C ?VA;O 3> >DB0;L <>;>3VG=>3> 70AB>AC20==O =87L:89. V2=V ?V:>28E :>=F5=B@0FV9 C ?;072V :>;820NBLAO 2V4 220 4> 888 ?3/<; (C A5@54=L® C :>6=5 >:> 4 @078 =0 4>1C ?>A;V4>2=> ?@>BO3<< 42>E 4=V2.

5:A0<5B07>= 282>48BLAO 7 >@30=V7< <5B01>;V7 60 % 4>78 284V;OTBLAO C A5GC C 283;O4V 6-β-3V4@>:A845:A0<5B07>=C. 57 - 3-4 3>48=8. 5:A0<5B07>= ?@81;87=> =0 77-84 % 72O7CTBLAO 7 0;L1C< A8@>20B:8 :@>2V. ;V@5=A :>;820TBLAO 2V4 0,111 4> 0,225 ;/3>4/:3 B0 >1T @>7?>4V;C :>;820TBLAO 2V4 0,576 4> 1,15 ;/:3. V>4>ABC?=VABL ?@8 ?5@>@0;L=>AC20==V AB0=>28BL ?@81;87=> 70 %.

">1@0

;V=VG=V D0@<0:>:V=5B8G=V 4>A;V465==O >G=>W <07V "!" =5 ?@>2>48;8AO. 4=0: 4>A;V465==O, ?@>2545=V 7 >G=8<8 :@0?;O<8 "!" , ?>:070;8, I> A8AB5<=89 2?;82 B>1@03> >DB0;L<>;>3VG=>3> 70AB>AC20==O =87L:89. V2=V :>=F5=B@0FVW B>1@02V =5 ?V44020;8AO :V;L:VA=> 70AB>A>2C20;8 >G=V :@0?;V "!" ?> >4=V9 :@0?;V C :>6=5 >:> G>B8@8 @078 =0 4>1C ?>A;V4>2=> ?@>B03>< 42>E 4=V2. 091V;LH89 28282 0,25

">1@0 B0 5:AB5=A82=> 5:A:@5BCTBLAO C A5GC H;OE<< 3;><5@C;O@=>W DV;LB@0FVW 3>;>2=8< G8=>< C =575=>4 =0?V2282545==O 7 ?;07<8 AB0=>28BL ?@81;87=> 2 3>48=8 7 ;:V@5=A< 0,04 ;/3>4/:3 B0 >1T<>< @>7?>4V;C 0,26 ;/:3. 2O7C20==O 1V;:0 ?;07<8 7 B>1@0< T =57=0G=8< <5=H5 =V6 10 %. V>4>ABC?=VABL ?@8 ?5@>@0;L=>AC20==V B>1@0

>.:V=VG=V 40=V 7 157?5:8

0=V I>4> 157?5:8

0=V 7 A8AB5<=>W B>:A8G=>ABV 0:B82=8E @5G>28= T 4>1@5 282G5=8<8. !8AB5<=89 2?;82 B>1@0 :A8G=8E 4>70E, O:V =01030B> ?5@528ICNBL 4>7C ?@8 AC20==V 2 >:>, <>65 1CB8 ?>2O70=89 V7 =5D@>B>:A8G=VABN B0 >B>B>:A8G=VABN. !8AB5<=89 2?;82 45:A0<5B07>=C <>65 1CB8 ?>2O70=89 7 5D5:B0<8, I> <0NBL 2V4=>H5==O 4> 3;N:>:>@B8:>AB5@>W4=>3> 48A10;0=AC. >A;V465==O B>:A8G=>ABV ?>2B>@=8E 4>7 >G=8E :@0?5;L "!" C :@>;V2 28O28;8 A8AB5<=V 5D5:B8, ?>2O70=V 7 :>@B8:>AB5@>W40<8, 0;5 =02VBL C 4>70E, I> VAB>B=> ?5@528ICNBL 4>7C 4;O ;N48=8, F59 ?@>O2 <0T =57=0G=C ;:V=VG=C @5;520=B=VABL. @870AB>AC20==V "!" C @5:><5=4>20=8E 4>70E 28=8:=5==O F8E 5D5:BV2 <0;>9<>2V@=5.

CB035==VABL

>A;V465==O *in vitro* B0 *in vivo* :>6=>W 7 4VNG8E @5G>28= W 4VW =5 28O28;8.

"5@0B>35==VABL

">1@0=8:0T :@V7L ?;0F5=BC C :@>2>>1V3 ?;>40 B0 =02:>;>?;V4=V 2>48. >A;V465==O =0 B20@8=0E ?@8 A8AB5<=>AC20==V 203VB=8< B20@8=0< 25;8:8E 4>7 B>1@0@30=>35=57C 28O28;8 =8@:>2C B>:A8G=VABL B0 >B>B>:A8G=VABL ?;>40. =HV 4>A;V465==O, O:V 1C;8 ?@>2545=V =0 IC@0E B0 :@>;OE V7 70AB>AC20==O< B>1@070E ?>=04 100 <3/:3/45=L ?@8 ?0@5=B5@0;L=>

C;> 2AB0=>2;5=>, I> ?V4 G0A 4>A;V465=L =0 B20@8=0E :>@B8:>AB5@>W48 <0;8 B5@0B>35==89 2?;82. 0AB>AC20==O 2 >:> 0,1 % 45:A0<5B07>=C 203VB=8< :@>;O< ?@8725;> 4> 71V;LH5==O 28?04:V2 ?>@CH5==O @>728B:C ?;>40 B0 70B@8CB@>1=>3> @>728B:C. 0B@8728B:C ?;>40 B0 71V;LH5==O 28?04:V2 A<5@B=>ABV A?>AB5@V30;8AO C IC@V2 ?@8 B@820;V9 B5@0?VW 45:A0<5B07>=>

"!" A;V4 70AB>A>2C20B8 ?V4 G0A 203VB=>ABV BV;L:8 B>4V, O:I> ?>B5=V9=0 :>@8ABL 2V4 70AB>AC20==O ?@5?0@0BC ?5@528IC20B8<5 ?>B5=V9=89 @878: 4;O ?;>40.

5 ?@>2>48;>AO 1C4L-O:8E 4>A;V465=L 4;O >FV=:8 :0=F5@>35==>W 4VW "!"C®.

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

>:070==O.

0?0;5==O >G59 C ?0FVT=BV2, GCB;828E 4> AB5@>W4V2, ?@8 O:8E ?>:070=5 70AB>AC20==O
:>@B8:>AB5@>W4V2 B0 VA=CT ?>25@E=520 10:B5@V0;L=0 V=D5:FVO 01> @878: @>728B:C
10:B5@V0;L=>W V=D5:FVW >:0. &V 70?0;L=V ?@>F5A8 <>6CBL 28=8:=CB8 ?VA;O EV@C@3VG=>3>
2B@CG0==O (2840;5==O :0B0@0:B8) 01> <>6CBL 1CB8 A?@8G8=5=V V=D5:FVTN, ?>B@0?;O==O< 2
>:> AB>@>==L>3> BV;0 01> >G=>N B@02<>N.

@>B8?>:070==O.

- V428I5=0 GCB;82VABL 4> 4VNG8E @5G>28= 01> 4> 1C4L-O:>3> :>5=B0 ?@5?0@0BC.
- 5@0B8B, A?@8G8=5=89 2V@CA<< herpes simplex.
- >@>2OG0 2VA?0, 2VB@O=0 2VA?0 B0 V=HV 2V@CA=V V=D5:FVW @>3V2:8 B0 :>=N=:B828.
- @81:>2V 70E2>@N20==O AB@C:BC@ >:0.
- V:>10:B5@V0;L=V V=D5:FVW >:0.

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

4=>G0A=5 ?@87=0G5==O AB5@>W4V2 4;O 3> 70AB>AC20==O B0 4;O 3> 70AB>AC20==O <>65
71V;LH8B8 @878: 28=8:=5==O CA:;04=5=L ?@8 703>T==V @0= @>3V2:8. !C?CB=T B0/01> ?>A;V4>2=5
70AB>AC20==O 0=B81V>B8:V2 3@C?8 03;V:>784V2 (B0:8E O: B>1@03> 70AB>AC20==O, O:V <0NBL
B>:A8G=89 (H:V4;8289) 2?;82 =0 =5@2>2C A8AB5@30=8 A;CEC 01> =8@:8, <>65 ?@8725AB8 4>
048B82=>W B>:A8G=>ABV, B>F5 <>6;82>, A;V4 C=8:0B8 B0:>3> 70AB>AC20==O.

/:I> 70AB>A>2CTBLAO 1V;LH5 >4=>3> >DB0;L<>;>3VG=>3> 70A>1C, V=B5@20; AC20==O< ?>28=5=
AB0=>28B8 =5 <5=H5 5 E28;8=. G=V <07V A;V4 70AB>A>2C20B8 2 >AB0==N G5@3C.

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

"V;L:8 4;O >DB0;L<>;>3VG=>3> 70AB>AC20==O.

45O:8E ?0FVT=BV2 <>6;820 ?V428I5=0 GCB;82VABL 4> 03;V:>784V2, I> 70AB>A>2CNBLAO . #
@07V 28=8:=5==O @50:FVW ?V428I5=>W GCB;82>ABV A;V4 ?@8?8=8B8 70AB>AC20==O
?@5?0@0BC.

>6;825 28=8:=5==O ?5@5E@5A=>W ?V428I5=>W GCB;82>ABV 4> V=H8E 03;V:>784V2. !;V4
@>73;O=CB8 2V@>3V4=VABL B>3>, I> ?0FVT=B8 7 ?V428I5=>N GCB;82VABN 4> B>1@0
AC20==V <>6CBL B0:>6 1CB8 GCB;828<8 V 4> V=H8E 03;V:>784V2, O:V ?@87=0G0NBLAO 01>
A8AB5<=>.

>2V4><;O;>AO ?@> A5@9>7=V ?>1VG=V @50:FVW, 2;:NG0NG8 =59@>B>:A8G=VABL,
>B>B>:A8G=VABL B0 =5D@>B>:A8G=VABL, C ?0FVT=BV2, O:V >B@8;V3>7840<8. @8
>4=>G0A=>AC20==V 7 A8AB5<=8<8 03;V:>7840<8 A;V4 1CB8 >15@56=8<.

"@820;5 ;V:C20==O :>@B8:>AB5@>W40<8 4;O 3> >DB0;L<>;>3VG=>3> 70AB>AC20==O <>65
?@8725AB8 4> >G=>W 3V?5@B5=7VW B0/01> 3;0C:<<8 7 CH:>465==O< 7>@>2>3> =5@20,
?>3V@H5==O< 3>AB@>B8 7>@C B0 ?>;O 7>@C, 0 B0:>6 4> CB2>@5==O AC1:0?AC;O@=>W
:0B0@0:B8 704=L>W :0<5@8 >:0. # ?0FVT=BV2, O:8< B5@0?VN :>@B8:>AB5@>W40<8
70AB>A>2CNBL 2 >:> B@820;>, =5>1EV4=> @53C;O@=> B0 1030B>@07>2> :>=B@>;N20B8
2=CB@VH=L>>G=89 B8A:. A>1;82> F5 T 206;828< 4;O 4VB59, >A:V;L:8 @878: 28=8:=5==O
?V428I5=>3> 2=CB@VH=L>>G=>3> B8A:C, A?@8G8=5=>3> :>@B8:>AB5@>W40<8, <>65 1CB8
1V;LH8< C 4VB59 B0 7028B8AO @0=VH5, =V6 C 4>@>A;8E.

- 878: 28=8:=5==O ?V428I5=>3> 2=CB@VH=L>>G=>3> B8A:C, A?@8G8=5=>3>
:>@B8:>AB5@>W40<8, B0/01> @878: CB2>@5==O :0B0@0:B8, 7C<>2;5=>W 70AB>AC20==O<
:>@B8:>AB5@>W4V2, 71V;LHCTBLAO C AE8;L=8E 4> FL>3> ?0FVT=BV2 (=0?@8:;04 C
E2>@8E =0 FC:@>289 4V015B).
- >@B8:>AB5@>W48 <>6CBL 7<5=HC20B8 @578AB5=B=VABL 4> 10:B5@V0;L=>W, 3@81:>2>W
01> 2V@CA=>W V=D5:FV9 B0 702048B8 28O2;5==N B0:8E V=D5:FV9 V <0A:C20B8 ;;V=VG=V
>7=0:8 V=D5:FVW.
- @8 ABV9:>@5==V 28@07>: @>3V2:8 A;V4 2@0E>2C20B8 <>6;82VABL 3@81:>2>W V=D5:FVW. #
@07V 28=8:=5==O 3@81:>2>W V=D5:FVW B5@0?VN :>@B8:>AB5@>W40<8 A;V4 ?@8?8=8B8.

"@820;5 70AB>AC20==O 0=B81V>B8:V2, B0:8E O: B>1@0>@30=V71EV4=> @>7?>G0B8
2V4?>2V4=C B5@0?VN.

- >@B8:>AB5@>W48 4;O >DB0;L<>;>3VG=>3> 70AB>AC20==O <>6CBL A?>2V;L=N20B8
703>T==O @0= @>3V2:8. "0:>6 2V4<>, I> 4;O 3> 70AB>AC20==O C?>2V;L=NNBL 01> 70B@8
T==O @0=. 4=>G0A=5 ?@87=0G5==O 4;O 3> 70AB>AC20==O V AB5@>W4V2 4;O 3>
70AB>AC20==O <>65 71V;LH8B8 @878: 28=8:=5==O CA::04=5=L ?@8 703>T==V @0= (482.
@>74V; «□70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9»).
- @8 =0O2=>ABV 70E2>@N20=L, I> ?@872>4OBL 4> ?>B>=H0==O @>3V2:8 01> A::5@8, AC20==O
AB5@>W4V2 <>65 A?@8G8=8B8 ?5@D>@0FVN.
- 5 @5:><5=4CTBLAO =>A8B8 :>=B0:B=V ;V=78 ?V4 G0A ;V:C20==O 70?0;5==O 01> V=D5:FVW >:0.

0AB>AC20==O C ?5@V>4 203VB=>ABV 01> 3>4C20==O 3@C44N.

5?@>4C:B82=0 DC=:FVO

>A;V465==O 7 <5B>N >FV=:8 2?;82C =0 D5@B8;L=VABL C ;N48=8 ?@8AC20==V "!"C®, <07V >G=>W,
=5 ?@>2>48;8AO.

03VB=VABL

0=V I>4> 70AB>AC20==O B>1@0 45:A0<5B07>=C 203VB=8< 6V=:0< 2V4ACB=V 01> WE :V;L:VABL >1
<565=0. >A;V465==O =0 B20@8=0E ?@>45<>=AB@C20;8 @5?@>4C:B82=C B>:A8G=VABL ?VA;O
A8AB5<=>3> ?@87=0G5==O :>@B8:>AB5@>W4V2 V B>1@0. 5 @5:><5=4CTBLAO 70AB>A>2C20==O
?@5?0@0BC "!"® ?V4 G0A 203VB=>ABV.

>4C20==O 3@C44N

52V4><>, G8 ?>B@0?;OT B>1@0DB0;L<>;>3VG=>AC20==V. >@B8:>AB5@>W48 B0 B>1@0
B@0?;ONBL 2 3@C4=5 <>;>?VA;O A8AB5<=>3> 70AB>AC20==O. 5 <>6=0 28::NG0B8 @878:C 4;O
48B8=8, O:C 3>4CNBL 3@C44N.

A;V;L:8 1030B> ;V:0@AL:8E 70A>1V2 ?>B@0?;ONBL C 3@C4=5 <>;>:, A;V4 @>73;O=CB8
<>6;82VABL B82>3> ?@8?8=5==O 3>4C20==O 3@C44N =0 G0A 70AB>AC20==O "!"C®.

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.

"!"®, <07L >G=0, =5 <0T 01> <0T =57=0G=89 2?;82 =0 740B=VABL :5@C20B8 02B>B@0=A?>@B< 01>
V=H8<8 <5E0=V7<0<8. "825 70BC<0=5==O 7>@C 01> V=HV ?>@CH5==O 7>@C <>6CBL 2?;820B8 =0
740B=VABL :5@C20B8 02B>B@0=A?>@B< 01> V=H8<8 <5E0=V7<0<8. !:I> 70BC<0=5==O 7>@C
28=8:0T ?V4 G0A 70AB>AC20==O, ?0FVT=BC =5>1EV4=> 70G5:0B8, 4>:8 7V@ ?@>OA=8BLAO, ?5@H
=V6 :5@C20B8 02B>B@0=A?>@B< 01> V=H8<8 <5E0=V7<0<8.

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

;O >DB0;L<>;>3VG=>3> 70AB>AC20==O.

0AB>AC20==O 4>@>A:8<, 2::NG0NG8 ?0FVT=BV2 ;VB=L>3> 2V:C, B0 4VBO< 2V:<< 2V4 12 4> 18
@>:V2

525;8:C :V;L:VABL<07V (A268=>N ?@81;87=> 1,5 A<) A;V4 70AB>A>2C20B8 C :>=N=:B820;L=89 :(-:8)
C@065=>3> >:0 (>G59) 4> 3 01> 4 @07V2 =0 4>1C. '0AB>BC 70AB>AC20==O ?@5?0@0BC A;V4
?>ABC?>2> 7<5=HC20B8 ?@8 ?>;V?H5==V ;V=VG=8E >7=0.: !;V4 1CB8 C206=8< B0 =5 ?@8?8=OB8
B5@0?VN ?5@54G0A=>.

G=C <07L <>6=0 28:>@8AB>2C20B8 =0 =VG C ?>T4=0==V V7 70AB>AC20==O< >G=8E :@0?5;L "!"®
?@>BO3<< 4=O.

VA;O 70AB>AC20==O<07V @5:>5=4CTBLAO >15@56=> 70:@8B8 ?>2V:8. &5 7=86CT A8AB5<=C
01A>@1FVN ?@5?0@0BC, 22545=>3> 2 >:, I> 7<5=HCT 2V@>3V4=VABL 28=8:=5==O A8AB5<=8E
?>1VG=8E 5D5:BV2.

5:>5=4CTBLAO ?>ABV9=> :>=B@>;N20B8 2=CB@VH=L>>G=89 B8A.:

0AB>AC20==O 4VBO<

B@8<0=V 40=V ?V4B25@46CNBL 157?5:C B0 5D5:B82=VABL 70AB>AC20==O ?@5?0@0BC 4VBO<
2V:> 2V4 1 @>:C, O:8< 70AB>A>2C20;8 ?@5?0@0B ?@>BO3>< 7 4=V2 4;O ;V:C20==O ?>25@E=528E
70?0;5=L >:0 10:B5@V0;L=>3> ?>E>465==O.

>6;825 70AB>AC20==O 4VBO<, O:8< =5>1EV4=> ?@>25AB8 EV@C@3VG=5 2B@CG0==O 7 2840;5==O
:0B0@0:B8.

0AB>AC20==O ?@8 ?>@CH5==OE DC=:FVV ?5GV=:8 B0 =8@>:

"!® =5 4>A;V46C202AO 4;O FVTW :0B53>@VW ?0FVT=BV2. 4=0: G5@57 =87L:C A8AB5<=C
01A>@1FVN B>1@03> 70AB>AC20==O ?@5?0@0BC =5>1EV4=>ABV C :>@83C20==V 4>78 =5<0T.

!>AV1 70AB>AC20==O

)>1 ?>?5@548B8 701@C4=5==O =0:>=5G=8:0 B0 21EV4=> 4>B@815@56=>ABV V =5 B>@:0B8AO
?>2V:, ?@8;53;8E 4V;O=>: 01> V=H8E ?>25@E>=L =0:>=5G=8:> BC18.

"@8<0B8 BC1C IV;L=> 70:@8B>N.

VB8

57?5:0 B0 5D5:B82=VABL 70AB>AC20==O 4VBO< <>;>4H5 1 @>:C =5 2AB0=>2;5=V.
B@8<0=V 40=V ?V4B25@46CNBL 157?5:C B0 5D5:B82=VABL 70AB>AC20==O ?@5?0@0BC 4VBO<
2V:> 2V4 1 @>:C.

5@54>7C20==O.

2060NG8 =0 E0@0:B5@8AB8:8 40=>3> ?@5?0@0BC, ?@87=0G5=>3> 4;O 3> 70AB>AC20==O, =5
>GV:CTBLAO 1C4L-O:>3> B>:A8G=>3> 5D5:BC O: ?@8 9>3> 70AB>AC20==V 2 >DB0;L<>;>3VW 2
@5:><5=4>20=8E 4>70E, B0: V ?@8 28?04:>2>:>2BC20==V 27C20==O ?@5?0@0B>< "!® ?@8 AC20==V
28<8B8 =04;8H>: ?@5?0@0BC 7 >:0 (>G59) B5?;>N 2>4>N.

>6;82V ;:V=VG=V >7=0:8 B0 A8<8 ?5@54>7C20==O ?@5?0@0B>< (B>G:>289 :5@0B8B, 5@8B5<0,
?V428I5=0 A;L>7>B5G0, =01@O: B0 A25@1V6 ?>2V:)<>6CBL 1CB8 ?>4V1=8<8 4> ?>1VG=8E 5D5:BV2,
I> A?>AB5@V30;8AL C 45O:8E ?0FVT=BV2.

>1VG=V @50:FVW.

V4 G0A ?@>2545==O ;:V=VG=8E 4>A;V465=L =09G0ABVH8<8 ?>1VG=8<8 @50:FVO<8 1C;8 1V;L 2
>G0E, ?V428I5=89 2=CB@VH=L>>G=89 B8A., ?>4@07=5==O >G59 B0 A25@1V6 >G59, O:V 28=8:0;8 C
<5=H =V6 1% ?0FVT=BV2.

@8 ?@>2545==V ;:V=VG=8E 4>A;V465=L 7 >G=>N <077N "!® 1C;> >B@8<0=> ?>2V4><;5==O ?@>
=86G5707=0G5=V =0ABC?>V ?>1VG=V @50:FVW, O:V >FV=N20;8AO 70 B0:>N G0AB>B>N: 4C65
G0ABV (≥ 1/10); G0ABV (≥ 1/100 - < 1/10); =5G0ABV (≥ 1/1000 - < 1/100); ?>>48=>:V (≥ 10 000 - < 1/1
000); >48=8G=V (< 1/10 000). # <560E :>6=>W 3@C?8 ?>1VG=V 5D5:B8 ?@54AB02;5=V 2 ?>@O4:C 7
<5=H5==O WE ABC?5=O BO6:>ABV.

"01;8FO 1

;0A8 A8AB5< >@30=V2

>1VG=V @50:FVW

(2V4?>2V4=89 B5@(v.15.1))

>@CH5==O 7 1>:C >@30=V2 7>@C

5G0ABV: ?V428I5==O 2=CB@VH=L>>G=>3> B8A:C, 1V;L 2 >G0E, A25@1V6 >G59, 48A:>@B 2 >G0E, ?>4@07=5==O >G59.

>>48=>:V: :5@0B8B, 0;5@3VO >G59, 70BC<0=5==O 7>@C, ACEVABL >G59, 3V?5@5G59.

>@CH5==O 7 1>:C H;C=:>2>-.8H:>2>3> B@0:BC

>>48=>:V: 48A3527VO.

0 @57C;LB0B0<8 ?>AB<0@:5B8=3>28E 4>A;V465=L 1C;8 28O2;5=V =86G5707=0G5=V ?>1VG=V @50:FVW.

0 ?V4AB02V ?@54AB02;5=8E 40=8E =5<>6;82> @>7@0EC20B8 G0AB>BC WE 28=8:=5==O.

"01;8FO 2

;0A8 A8AB5<>@30=V2

>1VG=V @50:FVW

(2V4?>2V4=89 B5@

>@CH5==O 7 1>:C VW A8AB5<8

V?5@GCB;82VABL

>@CH5==O 7 1>:C =5@2>2>W A8AB5<8

□0?0<>@>G5==O, 3>;>2=89 1V;L

>@CH5==O 7 1>:C >@30=V2 7>@C

01@O: ?>2V:, 5@8B5<0 ?>2V:, 7>B5G0, :=N=:B820;L=V ?>@CH5==O, 3;0C:><0, :0B0@0:B0

>@CH5==O 7 1>:C H;C=:>2>-.8H:>2>3> B@0:BC

C4>B0, 48A:>@B C H;C=:C

>@CH5==O 7 1>:C H:V@8 B0 ?V4H:V@=>W ;:VB:>28=8

8A8?, =01@O: >1;8GGO, A25@1V6, 5@8B5<0

?8A 45O:8E ?>1VG=8E @50:FV9

"@820;5 70AB>AC20==O :>@B8:>AB5@>W4V2 2 >:> <>65 ?@8725AB8 4> ?V428I5==O

2=CB@VH=L>>G=>3> B8A:C 7 ?>40;LH8< CH:>465==O< 7>@>2>3> =5@20, ?>3V@H5==O<

3>AB@>B8 7>@C V ?>@CH5==O< ?>;O 7>@C, 0 B0:>6 4> CB2>@5==O 704=L>W AC1:0?AC;O@=>W :0B0@0:B8 B0 C?>2V;L=5==O 703>T==O @0=(482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

A:V;L:8 ?@5?0@0B @B8:>AB5@>W4, B> ?@8 =002=>ABV 70E2>@N20=L, I> ?@872>4OBL 4>

?>B>=H0==O @>3V2:8 01> A:;5@8, ?V428ICTBLAO @878: ?5@D>@0FVW >A>1;82> ?VA;O

4>23>B@820;>3> 70AB>AC20==O (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

>6;8289 @>728B>: 2B>@8==8E V=D5:FV9 ?VA;O 70AB>AC20==O :<1V=0FV9, I> @B8:>AB5@>W48

B0 0=B81=V @5G>28=8. @81:>2V V=D5:FVW @>3V2:8 >A>1;82> 0:B82=> @>72820NBLAO ?@8

B@820;>AC20==V AB5@>W4V2 (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

?0FVT=BV2, O:8< 74V9A=N20;8 A8AB5<=C B5@0?VN V7 70AB>AC20==O< B>1@07=V ?>1VG=V

@50:FVW, 2;;NG0NG8 =59@>B>:A8G=VABL, >B>B>:A8G=VABL V =5D@>B>:A8G=VABL.

5O:V ?>1VG=V @50:FVW, B0:V O: 01@07VO @>3V2:8, ?>3V@H5==O 7>@C, =01@O: :=N=:B828,

?>@CH5==O 7 1>:C ?>2V:, 284V;5==O 7 >G59, A25@1V6 ?>2V:, :@>?82O=:0, 45@<0B8B, <040@>7,

;59:>45@<0, ACEVABL H:V@8 A?>AB5@V30;8AL ?V4 G0A B5@0?VW B>1@0

>1VG=V @50:FVW, B0:V O: :5@0B>:=N=:B82VB, 7010@2;5==O @>3V2:8, D>B>D>1VO, CB2>@5==O

;CA>G>: ?> :@0OE ?>2V:, 7=865==O 3>AB@>B8 7>@C, 5@>7VO @>3V2:8, ?B>7 ?>2V:

A?>AB5@V30;8AL ?V4 G0A B5@0?VW 45:A0<5B07>=>

45O:8E ?0FVT=BV2 <>6;820 @50:FVO ?V428I5=>W GCB;82>ABV 4> 03;V:>784V2 ?@8 AC20==V (482.

@>74V; «A>1;82>ABV 70AB>AC20==O»).

"5@ABV.

2 @>:8. "5@3> 2V4:@8BBO BC18 - 1

#<>28 715@V30==O.

15@V30B8 ?@8 B5 25 °C.

5 70<>@>6C20B8.

15@V309B5 C ABC?=8E 4;O 4VB59. "@8<09B5 BC1C IV;L=> 70:@8B>N.

#?0:>2:0.

> 3,5 3 ?@5?0@0BC 2 0;N:A8D5=>;L=8< 2=CB@VH=V< ?>:@8BBO<, ?>;V5B8;5=>28< =0:>=5G=8:< B0
?>;V5B8;5=>28< :>2?0G:> 1 BC1V 2 :0@B>==V9 :>@>1FV 7 :0@B>=C ?0:C20;L=>3>.

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

0 @5F5?B>

8@>1=8:.

::>=-□C2@L>@/Alcon-Couvreur.

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

V9:A253 14, B-2870 CC@A, 5;L3VO/Rijksweg 14, B-2870 Puurs, Belgium.