

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

!□#  
(NEXIUM®)

!::04:

4VNG0 @5G>28=0: 57<<5?@07>;  
1 D;0:>=<5?@07>;C =0B@VN 42,5 <3, I> 5:2V20;5=B=> 57<<5?@07>;C 40 <3;  
4>?>28=8: 48=0B@VN 545B0B, =0B@VN 3V4@>:A84.

V:0@AL:0 D>@<0. >@>H>: 4;O @>7G8=C 4;O V=T:FV9 B0 V=DC7V9.  
A=>2=V DV78:>-EVABV: ?>@8AB0 3@C4:0 01> ?>@>H>: 1V;>3> 01> <0965 1V;>3> :>;L>@C.

\$0@<0:>B5@0?52B8G=0 3@C?0. 0A>18 4;O ;V:C20==O ?5?B8G=>W 28@07:8 B0  
30AB@>57>D0350;L=>W @5D;N:A=>W E2>@>18. >4 □"% A02B C05.

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

7><5?@07>; T S-V7<<5@><><5?@07>;C, I> ?@83=VGCT A5:@5FVN :8A;>B8 H;C=:>2>3> A>:C 70240:8  
A?5F8DVG=>-, V S-V7<<5@8 ><5?@07>;C <0NBL ?>4V1=C D0@<0:>;>3VG=C 0:B82=VABL.

VAF5 B0 <5E0=V7< 4VW

7><5?@07>; O2;OT A>1>N A;01:C >A=>2C, I> :>=F5=B@CTBLAO B0 ?5@5B2>@NTBLAO =0 0:B82=C  
D>@ :8A;>28IV A5:@5B>@=8E :0=0;LFV2 ?0@VTB0;L=8E ;;VB8=, 45 V=3V1CT D5@<5=B + +-"\$-07C  
:8A;>B=C ?>20=C A5:@5FVN :8A;>B8.

?;82 =0 A5:@5FVN H;C=:>2>3> A>:C

'5@57 5 4=V2 ?5@>@0;L=>3> ?@89> 20 <3 B0 40 <3 57><5?@07>;C @V25=L @H;C=:0 28I5 4  
715@V302AO 2V4?>2V4=> 2 A5@54=L>BO3<< 13 3>48= B0 17 3>48= ?@>BO3<< 24-3>48==>3>  
V=B5@20;C C ?0FVT=BV2 V7 A8<0B8G=>N % (30AB@>57>D0350;L=>W @5D;N:A=>W E2>@>18).

D5:B ?>4V1=89 =570;56=> 2V4 B>3>, 70AB>A>2CTBLAO 57><5?@07>; ?5@>@0;L=> G8

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

0 4>?><>3>N AUC O: >?>A5@54:>20=>3> ?0@0<5B@0 :>=F5=B@0FVW ?@5?0@0BC C ?;072V 1C;>  
?@>45<>=AB@>20=> 70;56=VABL

@8 2=CB@VH=L>25==><5?@07>;C 74>@>28< 4>1@>2>;LFO< C 4>7V 80 <3 C 283;04V 1>;NA=>W  
V=DC7VW B@820;VABN 30 E28;8= V7 ?>40;LH8< 70AB>AC20==O< ?@5?0@0BC C 283;04V B@820;>W

2=CB@VH=L>25==>W V=DC7VW 7V H284:VABN 8<3/3>48=C B@820;VABN 23,5 3>48=8 @V25=L  
@H;C=:0 28I5 4 B0 28I5 6 715@V302AO 2V4?>2V4=> 2 A5@54=L>BO3<< 21 3>48=8 B0 11-13

3>48=?@>BO3<< 24-3>48==>3> V=B5@20;C.

"5@0?52B8G=89 5D5:B ?@83=VG5==O A5:@5FVW :8A;>B8

@8 ?5@>@0;L=>AC20==V 57><5?@07>;C 2 4>7V 40 <3 ?@81;87=> 78 % ?0FVT=BV2 V7 @5D;N:A=8<  
57>D03VB><>4C6CNBL G5@57 4 B86=V, 93 % G5@57 8 B86=V2 ;V:C20==O.

# @0=4>20=>42V9=>.:>=B@>;L>20=>A;V465==V ?0FVT=BV2 V7 5=4>A:>?VG=> 4>2545=>N

?5?B8G=>N 28@07:>N ;:0AC 0, 1, 0 G8 1 (9 %, 43 %, 38 % B0 10 % 2V4?>2V4=>) 70 \$>@>5AB<< @0=4>  
3@C? 70AB>AC20==O ?@5?0@0BC 5:AVC<, @>7G8= 4;O V=DC7V9 (n=375), 01> ?;0F51> (n=389). VA;O  
5=4>A:>?VG=>3> 35<>AB07C ?0FVT=B0< 22>48;8 01> 57><5?@07>; C 4>7V 80 <3 C 283;04V

2=CB@VH=L>25==>W V=DC7VW B@820;VABN 30 E28;8= V7 ?>40;LH>N B@820;>N V=DC7VTN 7V  
H284:VABN 8<3/3>48=C 01> ?;0F51> ?@>BO3<< 72 3>48=. VA;O ?>G0B:>2>3> 72-3>48==>3> ?5@V>4C

2AVE ?0FVT=BV2 ?5@52>48;8 =0 2V4:@8B89 ?5@>@0;L=89 ?@89< ?@5?0@0BC 5:AVC< C 4>7V 40  
<3 ?@>BO3<< 27 4=V2 4;O ?@83=VG5==O :8A;>B=>W A5:@5FVW. '0AB>B0 ?>2B>@=>W :@>2>B5GV

?@>BO3<< 3 4V1 AB0=>28;0 5,9 % C 3@C?V ?@89>. '5@57 30 4=V2 ?VA;O B5@0?VW G0AB>B0  
?>2B>@=8E :@>2>B5G C 3@C?V ?@89> AB0=>28;0 2V4?>2V4=> 7,7 % B0 13,6 %

=HV 5D5:B8, ?>2070=V V7 ?@83=VG5==O< A5:@5FVW :8A;>B8

# ?5@V>4 ;V:C20==O 0=B8A5:@5B>@=8<8 ?@5?0@0B0<8 @V2=V 30AB@8=C C A8@>20BFV  
7@>AB0NBL C 2V4?>2V4L =0 7=865==O A5:@5FVW :8A;>B8. V25=L E@>>3@0=V=C (CgA) B0:>6  
7@>AB0T 2=0A;V4>: 7<5=H5==O :8A;>B=>ABV H;C=:>2>3> A>:C.  
V428I5==O :V;L:>ABV 5=B5@>E@><0DV=>?>4V1=8E ;;VB8=, <>6;82? ?>2O70=5 7V 71V;LH5==O<  
@V2=O 30AB@8=C, A?>AB5@V30;>AO C 45O:8E ?0FVT=BV2 C ?5@V>4 4>23>B@820;>3> ;V:C20==O  
?5@>@0;L=8< 57<<5?@07>;>

0 D>=V 4>23>B@820;>3> ;V:C20==O ?5@>@0;L=8<8 0=B8A5:@5B>@=8<8 ?@5?0@0B0<8  
2V47=0G0;>AO 45O:5 7@>AB0==O G0AB>B8 CB2>@5==O H;C=:>28E 3;0=4C;O@=8E :VAB. &V 7  
;>3VG=8< =0A;V4:>< 28@065=>3> ?@83=VG5==O A5:@5FVW H;C=:>2>3> A>:C, <0NBL 4>1@>O:VA=C  
B0 >1>@>B=C ?@8@>4C.  
<5=H5==O :8A;>B=>ABV H;C=:>2>3> A>:C V7 1C4L-O:8E ?@8G8=, C B>: 70AB>AC20==O  
V=3V1VB>@V2 ?@>B==>W ?>48BL 4> 71V;LH5==O C H;C=:C :V;L:>ABV 10:B5@V9, I> 70728G09  
?@8ACB=V C H;C=:>2>-.8H:>2>@0<8 ?@>B==>W ?>65 45I> 71V;LHC20B8 @878: H;C=:>2>-.8H:>28E  
V=D5:FV9, 7C<>2;5=8E, =0?@8;:04, *Salmonella B0 Campylobacter*, V C 3>A?VB0;V7>20=8E ?0FVT=BV2,  
<>6;82>, B0:>6 *Clostridium difficile*

VB8  
57C;LB0B8, >B@8<0=V 2 E>4V 4>A;V465=L 70 CG0ABN ?0FVT=BV2 48BOG>3> 2V:C, ?>:07CNBL, I>  
4>78 57<<5?@07>;C 0,5 <3/:3 V 1,0 <3/:3 C =5<>2;OB 2V:>< <1 2V4=> 7=86CNBL A5@54=V9 2V4A>B>:  
G0AC 7 2=CB@VH=L>AB@02>EV4=8< @<4.  
@>DV;L 157?5:8 70AB>AC20==O ?@5?0@0BC 28O282AO ?>4V1=8< 4> B>3>, I> A?>AB5@V302AO C  
4>@>A;8E.

\$0@<0:>:V=5B8:0.  
>7?>4V;  
#02=89 >1T< @>7?>4V;C C AB0FV>=0@=>@>28E 4>1@>2>;LFV2 AB0=>28BL ?@81;87=> 0,22 ;/:3  
<0A8 BV;0. 7<>5?@07>; =0 97 % 72O7CTBLAO V7 1V;;:0<8 ?;07<8 :@>2V.  
5B01>;V7< B0 282545==O  
7><5?@07>; ?>2=VABN <5B01>;V7CTBLAO A8AB5<>N F8B>E@>2=0 G0AB8=0 <5B01>;V7<5?@07>;C  
70;568BL 2V4 ?>;V<>@D=>3> CYP2C19, I> 2V4?>2V40T 70 CB2>@5==O 3V4@>:A8- B0 45A<5B8;  
<5B01>;VBV2 57<<5?@07>;C. 5HB0 <5B01>;V7N A?5F8DVG=>N V7>D>@<>N, CYP3A4, I>  
2V4?>2V40T 70 CB2>@5==O 57<<5?@07>;C AC;LD>=C, >A=>2=>3> <5B01>;VBC C ?;072V.

86G5=02545=V ?0@0<5B@8 2V4>1@060NBL ?5@5206=> D0@<0:>:V=5B8:C C >AV1 V7 DC=:FV>=0;L=8  
< CYP2C19 D5@<5=B><, B>1B> H284:8E <5B01>;V70B>@V2.  
030;L=89 ?;07<>289 ;:V@5=A AB0=>28BL ?@81;87=> 17 ;/3>48=C ?VA;O @07>2>W 4>78 B0 ?@81;87=> 9  
;/3>48=C ?VA;O ?>2B>@=>3> 70AB>AC20==O. 5@V>4 =0?V2282545==O ?@5?0@0BC V7 ?;07<8  
AB0=>28BL ?@81;87=> 1,3 3>48=8 ?@8 ?>2B>@=>AC20==V >48= @07 =0 4>1C. 030;L=0 5:A?>78FVO  
(AUC) 7@>AB0T ?@8 ?>2B>@=>AC20==V 57<<5?@07>;C. &5 7@>AB0==O 70;568BL 2V4 4>78 B0  
?@872>48BL CB2>@5==O =5;V=V9=>W 70;56=>ABV 7>N B0 AUC ?VA;O ?>2B>@=>3>  
70AB>AC20==O. "0:0 70;56=VABL 2V4 G0AC B0 4>78 7C<>2;5=0 7=865==O< ?@5A8AB5<=>3>  
<5B01>;V7, 2V@>3V4=>, ?@83=VG5==O< D5@<5=BC CYP2C19 57<<5?@07>;>< B0/01> 9>3>  
AC;LD>=>28< <5B01>;VB><.  
7><5?@07>; ?>2=VABN 282>48BLAO V7 ?;07<8 <0<8, V B5=45=FVW 4> 9>3> =0:>?8G5==O 2 >@30=V7  
AC20==V >48= @07 =0 4>1C =5 A?>AB5@V30TBLAO.  
@8 ?>2B>@=>AC20==V ?@5?0@0BC 2 4>70E 40 <3 C 283;O4V 2=CB@VH=L>25==8E V=T:FV9  
A5@54=O <0:A8<0;L=0 :>=F5=B@0FVO 9>3> C ?;0728BL ?@81;87=> 13,6 AC20==V ?>@V2=O=> V7  
?5@>@0;L=8< ?@89><>> ;V=V9=5 4>7>70;56=5 7@>AB0==O 5:A?>78FVW ?@8 22545==V 57>  
<5?@07>;C C 283;O4V 2=CB@VH=L>25==>W V=DC7VW B@820;VABN 30 E28;8= (C 4>7V 40<3, 80 <3  
01> 120 <3) V7 ?>40;LH8< 9>3> 22545==O< C 283;O4V B@820;>W V=DC7VW (7V H284:VABN 4<3/3>4  
01> 8 <3/3>4) ?@>BO3>< 23,5 3>48=8.  
A=>2=V <5B01>;VB8 57<<5?@07>;C =5 ?;820NBL =0 A5:@5FVN H;C=:>2>3> A>:C. 0965 80 %  
?5@>@0;L=>W 4>78 57<<5?@07>;C 282>48BLAO C 283;O4V <5B01>;VBV2 V7 A5G5N, @5HB0 V7 :0;>  
W A?>;C:8 282>48BLAO V7 A5G5N.

0FVT=B8 >A>1;828E 3@C?

@81;87=> 2,9 ±1,5 % =0A5;5==O =5 <0T DC=:FV>=0;L=>3> D5@<5=BC CYP2C19 V =07820TBLAO ?>2V;L=8<8 <5B01>;V70B>@0<8. # F8E >AV1 <5B01>;V7< 57><5?@07>;C, 9<>2V@=>, :0B0;V7CTBLAO ?5@5206=8< G8=>< CYP3A4. VA;O 1030B>@07>2>3> ?5@>@0;L=>3> ?@89> <5?@07>;C C 4>7V 40 <3 >48= @07 =0 4>1C A5@54=O 7030;L=0 5:A?>78FVO 1C;0 ?@81;87=> =0 100 % 28I5N C ?>2V;L=8E <5B01>;V70B>@V2, =V6 C >AV1 V7 DC=:FV>=0;L=8< D5@<5=B<< CYP2C19 (H284:8E <5B01>;V70B>@V2). !5@54=O <0:A8<0;L=0 :>=F5=B@0FVO C ?;07 =0 60 %. >4V1=V 2V4ABV A?>AB5@V30;8AO V ?@8 2=CB@VH=L>25==><5?@07>;C. &V 40=V =5 28<030NBL 77C20==V 57> <5?@07>;C.

5B01>;V7< 57><5?@07>;C =57=0G=8< G8=>< 7AV1 (71-80 @>:V2). VA;O >4=>@07>2>3> ?5@>@0;L=>3> ?@89><5?@07>;C C 4>7V 40 <3 A5@54=O 7030;L=0 5:A?>78FVO C 6V=>: ?@81;87=> =0 30 % 28I0, =V6 C G>;>2V:V2. 0;56=>W 2V4 AB0BV @V7=8FV =5 2V47=0G0TBLAO ?@8 ?>2B>@=>AC20==V ?@5?0@0BC >48= @07 =0 4>1C. >4V1=V 2V4ABV A?>AB5@V30;8AO ?@8 2=CB@VH=L>25==>AC20==V 57><5?@07>;C. &V 40=V =5 2?;820NBL =0 4>7C20==O 57><5?@07>;C.

5B01>;V7< 57><5?@07>;C C ?0FVT=BV2 V7 ;53:8<8 01> ?>: G>3> 7030;L=0 5:A?>78FVO 57><5?@07>;C 7@>AB0T 242VGV. ">. # @07V 28@07:8, I> :@>2>B>G8BL, B0 BO6:8E ?>@CH5==L DC=:FVW ?5GV=:8 ?VA;O 22545==O ?>G0B:>2>W 1>;NA=>W 4>78 80<3 22545==O ?@5?0@0BC C 283;04V B@820;>W 2=CB@VH=L>25==>W V=DC7VW 7V H284:VABN<0:A8□7><5?@07>; 01> 9>3> >A=>2=V <5B01>;VB8 =5 28O2;ONBL B5=45=FVW 4> =0:>?8G5==O ?@8 70AB>AC20==V >48= @07 =0 4>1C.

5 ?@>2>48;>AO 4>A;V465=L 70 CG0ABN ?0FVT=BV2 7V 7=865=>N DC=:FVTN =8@>:. A:V;L:8 =8@:8 2V4?>2V40NBL 70 282545==O <5B01>;VBV2 57><5?@07>;C, 0;5 =5 70 282545==O >A=>2=>W A?>;C:8, 7 GV:CTBLAO C ?0FVT=BV2 V7 ?>@CH5==O< DC=:FVW =8@>:.

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

**>:070==O.**

>@>A;V

- =B8A5:@5B>@=0 B5@0?VO, C @07V, :>;8 =5<>6;82> 70AB>A>2C20B8 ?5@>@0;L=89 H;OE 22545==O, =0?@8:;04:
- 30AB@>57>D0350;L=0 @5D;N:A=0 E2>@>10 C ?0FVT=BV2 7 57>D03VB<< B0/01> BO6:8<8 A8 <0<8 @5D;N:AC;
- ;V:C20==O 28@07>: H;C=:0, ?>2O70=8E 7 B5@0?VTN =5AB5@>W4=8<8 ?@>B870?0;L=8<8 70A>10<8 (□ );
- ?>?5@5465==O 28@07>: H;C=:0 B0 420=04FOB8?0;>W :8H:8, ?>2O70=8E 7 B5@0?VTN , C ?0FVT=BV2, O:V 2E>4OBL 4> 3@C?8 @878:C.
- >@>B:>B@820;5 ?V4B@8<0==O 35<>AB07C B0 ?@>DV;0:B8:0 ?>2B>@=>W :@>2>B5GV C ?0FVT=BV2 ?VA;O 5=4>A:>?VG=>3> ;V:C20==O 3>AB@>W :@>2>B5GV 2=0A;V4>: 28@07:8 H;C=:0 01> 420=04FOB8?0;>W :8H:8.

VB8 2V:>< 2V4 1 4> 18 @>:V2

- =B8A5:@5B>@=0 B5@0?VO, C @07V, :>;8 =5<>6;82> 70AB>A>2C20B8 ?5@>@0;L=89 H;OE 22545==O, =0?@8:;04:
- 30AB@>57>D0350;L=0 @5D;N:A=0 E2>@>10 (%) C ?0FVT=BV2 7 5@>782=8< @5D;N:A=8< 57>D03VB<< B0/01> BO6:8<8 A8<0<8 @5D;N:AC.

**@>B8?>:070==O.**

V428I5=0 GCB;82VABL 4> 4VNG>W @5G>28=8 57><5?@07>;C, V=H8E 70;V2 01> 1C4L-O:>W V7 4>?> 28= FL>3> ;V:0@AL:>3> 70A>1C.

7><5?@07>; =5 A;V4 70AB>A>2C20B8 >4=>G0A=> 7 0B070=02V@><, =5;DV=02V@>< (482. @>74V; «70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9»).

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

>A;V465==O 270T<>4VW ?@>2>48;8AO ;8H5 C 4>@>A;8E.

?;82 57><5?@07>;C =0 D0@<0:>:V=5B8:C V=H8E ;V:0@AL:8E 70A>1V2

V:0@AL:V 70A>18, 2A<>:BC20==O O:8E 70;568BL 2V4 @

@83=VG5=O H;C=:>2>W A5:@5FVW =0 D>=V B5@0?VW 57<5?@07>;<> B0 V=H8<8 (V=3V1VB>@ ?@>B>=>W ?> <>65 ?@872>48B8 4> ?>A;01;5=O 01> ?>A8;5=O 2A<>:BC20=O ;V:0@AL:8E 70A>1V2, 01A>@1FVO O:8E 70;568BL 2V4 @V2=O @H;C=:>2>3> A>:C. /: V ?@8 70AB>AC20=V V=H8E ;V:0@AL:8E 70A>1V2, I> 7<5=HCNBL :8A;>B=VABL H;C=:>2>3> A>:C, 2A<>:BC20=O B0:8E ?@5?0@0BV2, O: :5B>:=07>;, VB@0:=07>; B0 5@;>B8=V1, <>65 ?>A;01;N20B8AO, 0 2A<>:BC20=O 4 83>:A8=C ?>A8;N20B8AO 2 ?5@V>4 70AB>AC20=O 57<5?@07>;C. @8 AC?CB=L>AC20=V > <5?@07>;C (20 <3 =0 4>1C) B0 483>:A8=C C 74>@>28E 4>1@>2>;LFV2, 1V>4>ABC?=VABL 483>:A8=C 7@>AB0;0 =0 10 % (4> 30 % C 42>E V7 45AOB8 CG0A=8:V2). ">:A8G=V 5D5:B8 483>:A8=C 2V47=0G0;8AO 7@V4:0. 4=0: A;V4 4>B@815@56=>ABV ?@8 70AB>AC20=V 28A>:8E 4>7 57> <5?@07>;C ?0FVT=B0< ;VB=L>3> 2V:C. !;V4 ?>A8;8B8 <=>VB>@8=3 :>=F5=B@0FVW 483>:A8=C C :@>2V ?0FVT=B0.

V47=0G5=0 270T<>4VO <>5?@07>;C V7 45O:8<8 V=3V1VB>@0<8 ?@>B5078. ;V=VG=0 7=0GCIVABL B0 <5E0=V7<8 F8E 270T<>4V9 =5 702648 2V4>2>3> A>:C 2 ?5@V>4 B5@0?VW <5?@07>;<> <>65 7V <5E0=V7<8 270T<>4VW <>6;82V G5@57 ?@83=VG5=O CYP2C19. =865=O A8@>20B:>28E @V2=V2 0B070=02V@C B0 =5;DV=02V@C 2V47=0G0;>AO ?@8 >4=>G0A=>AC20=V <5?@07>;C, B> 70AB>A>2C20B8 FV ?@5?0@0B8 =5 @5:>5=4CTBLAO. !C?CB=T 70AB>AC20=O <5?@07>;C (40 <3 >48= @07 =0 4>1C) 7 0B070=02V@>< 300 <3/@8B>=02V@>< 100 <3 C 74>@>28E 4>1@>2>;LFV2 A?@8G8=O;> 7=0G=5 7=865=O 5:A?>78FVW 0B070=02V@C (7=865=O AUC, C<sub>max</sub> B0 C<sub>min</sub> ?@81;87=> =0 75 %). V428I5=O 4>78 0B070=02V@C 4> 400 <3 =5 :> 2?;82 <5?@07>;C =0 5:A?>78FVN 0B070=02V@C. !C?CB=T 70AB>AC20=O <5?@07>;C (20 <3 =0 4>1C) 7 0B070=>2V@>< 400 <3/ @8B>=02V@>< 100 <3 C 74>@>28E 4>1@>2>;LFV2 7=86C20;> 5:A?>78FVN 0B070=02V@C ?@81;87=> =0 30 % ?>@V2=O=> 7 5:A?>78FVTN, 2V47=0G5=>N ?@8 70AB>AC20=V 0B070=02V@C 300 <3/ @8B>=02V@C 100 <3 >48= @07 =0 4>1C 157 70AB>AC20=O <5?@07>;C 2 4>7V 20 <3 =0 4>1C. !C?CB=T 70AB>AC20=O <5?@07>;C (40 <3 =0 4>1C) 7<5=HC20;> A5@54=V 7=0G5=O AUC, C<sub>max</sub> B0 C<sub>min</sub> =5;DV=02V@C =0 36-39%, 0 A5@54=V 7=0G5=O AUC, C<sub>max</sub> B0 C<sub>min</sub> D0@<0:>;>3VG=> 0:B82=>3> <5B01>;VBC 8 =0 75-92%.

V428I5=O :>=F5=B@0FVW A0:2V=02V@C (I> 70AB>A>2C202AO >4=>G0A=> 7 @8B>=02V@><) C A8@>20BFV (80-100 %) A?>AB5@V30;>AO ?@8 AC?CB=L>AC20=V <5?@07>;C (2 4>7V 40 <3 =0 4>1C). <5?@07>; C 4>7V 20 <3 =0 4>1C =5 2?;8202 =0 5:A?>78FVN 40@C=02V@C (I> 70AB>A>2C202AO >4=>G0A=> V7 @8B>=02V@><) B0 0T4=0=V V7 @8B>=02V@><). 7<5?@07>; C 4>7V 20 <3 =0 4>1C =5 2?;8202 =0 5:A?>78FVN 0T=0=V V7 @8B>=02V@>< G8 >:@5<>). 0AB>AC20=O <5?@07>;C 2 4>7V 40 <3/4>1C =5 7 5:A?>78FVN ;>?V=02V@C (C ?>T4=0=V V7 @8B>=02V@><). '5@57 ?>4V1=VABL D0@<0:>48=0

V:0@AL:V 70A>18, I> <5B01>;V7CNBLAO CYP2C19

7><5?@07>; ?@83=VGCT CYP2C19 >A=>2=89 D5@<5=B, I> <5B01>;V7CT 57<5?@07>;. ">T4=0=V 57><5?@07>;C V7 ;V:0@AL:8<8 70A>10<8, I> <5B01>;V7CNBLAO CYP2C19, B0:8<8 O: 4V075?0<, F8B0;>?@0<, VW= B>I>, :>=F5=B@0FVW F8E ?@5?0@0BV2 C ?;071CB8 ?>B@V1=8< 7<5=H5=O WE 4>7. !C?CB=V9 ?5@>@0;L=89 ?@89>< 30 <3 57><5?@07>;C ?@872>482 4> 7=865=O ;V@5=AC AC1AB@0BC CYP2C19 4V075?0 %. @8 AC?CB=L>@0;L=>AC20=V 40 <3 57><5?@07>;C B0 D5=VB>W=C, 2V E2>@8E =0 5?V;5?AVN 7@>AB0;8 =0 13%. 5:>5=4CTBLAO :>=B@;>N20B8 :>=F5=B@0FVW D5=VB>W=C C ?;07G0B:C B5@0?VW 57<5?@07>;<> B0 ?@8 WW ?@8?8=5=V. 0AB>AC20=O <5?@07>;C (40 <3 >48= @07 =0 4>1C) A?@8G8=O;> 7@>AB0=O C<sub>max</sub> B0 AUC<sub>t</sub> 2>@8:=07>;C (AC1AB@0BC CYP2C19) 2V4?>2V4=> =0 15% B0 41 % 2V4?>2V4=>. @8 AC?CB=L>@0;L=>AC20=V 40 <3 57><5?@07>;C ?0FVT=B0<8, O:V ?@89<0;8 20@D0@8= C @03> 4>A;V465=O, G0A 7AV40=O :@>2V 70;8H02AO C<560E V=B5@20;C ?@8?CAB8<8E 7=0G5=L. 4=0: C ?>AB<0@:5B8=3>289 ?5@V>4 =0 D>=V 70AB>AC20=O ?5@>@0;L=>3> 57><5?@07>;C 1C;8 2V47=0G5=V ;V;L:0 >:@5<8E 28?04:V2 ;V=VG=> 7=0GCI>3> ?V428I5=O ! ?@8 AC?CB=L>AC20=V F8E ?@5?0@0BV2. 5:>5=4CTBLAO ?@>2>48B8 <=>VB>@8=3 =0 ?>G0B:C B0 =0?@8:V=V AC?CB=L>3> 70AB>AC20=O 57><5?@07>;C B0 20@D0@8=C 01> V=H8E :C<0@8=>28E ?>EV4=8E. @8 >4=>G0A=>AC20=V 57><5?@07>;C ?>2V4><;O;>AL ?@> ?V428I5=O @V2=O B0:@>;V20BFV.

<5?@07>;, O: V 57<5?@07>;, T V=3V1VB>@< CYP2C19. # 74>@>28E 4>1@>2>;Lfv2 C E>4V  
?5@5E@5A=>3> 4>A;V465==O 70AB>AC20==O ><5?@07>;C 2 4>7V 40 <3 ?@872>48;> 4> 7@>AB0==O  
C<sub>max</sub> B0 AUC F8;>AB07>;C 2V4?>2V4=> =0 18% B0 26%, 0 >4=>3> V7 9>3> 0:B82=8E <5B01>;VBV2 =0  
29 % B0 69 %.

!C?CB=V9 ?5@>@0;L=89 ?@89>< 40 <3 57><5?@07>;C B0 F870?@84C C 74>@>28E 4>1@>2>;Lfv2  
?@872>482 4> 71V;LH5==O ?;>IV ?V4 :@82>N 70;56=>ABV :>=F5=B@0FVW 2V4 G0AC (AUC) =0 32 %,  
0 ?5@V>4C =0?V2282545==O (t<sub>1/2</sub>) =0 31%, 0;5 7=0G=>3> ?V428I5==O <0:A8<0;L=>W :>=F5=B@0FVW  
F870?@84C C ?;072V 2V47=0G5=> =5 1C;>. 525;8:5 ?>4>265==O V=B5@20;C Q" c, I> 2V47=0G0;>AO  
?@8 70AB>AC20==V F870?@84C >:@5<>, =5 71V;LHC20;>AO ?@8 70AB>AC20==V F870?@84C C :>  
<1V=0FVW 7 57><5?@07>;>

C;> ?>:070=> I> 57><5?@07>;, ;V=VG=> 7=0GCI5 =5 2?;8202 =0 D0@<0:>:V=5B8:C 0<>:A8F8;V=C 01>  
EV=V48=C.

>A;V465==O 270T<>4VW *in vivo* V7 70AB>AC20==O< D>@<8 ?@5?0@0BC 4;O 2=CB@VH=L>25==>3>  
22545==O C 25;8:8E 4>70E (80 <3 + 8 <3/3>48=C) =5 ?@>2>48;8AO. ?;82 57><5?@07>;C =0 ;V:0@AL:V  
70A>18, I> <5B01>;V7CNBLAO CYP2C19, =0 D>=V B0:>3> @568I>4> @>728B:C =51060=8E O28I.  
V4 G0A ?5@5E@5A=>3> ;V=VG=>3> 4>A;V465==O ;;>?V4>3@5; (C =020=B06C20;L=V9 4>7V 300 <3  
V7 ?>40;LH8< 70AB>AC20==O< ?> 75 <3/4>1C) 70AB>A>2C20;8 >:@5<> B0 C ?>T4=0==V V7 >  
<5?@07>;< (?> 80 <3 >4=>G0A=> V7 ;;>?V4>3@5;>) ?@>BO3< 5 4=V2. :A?>78FVO 0:B82=>3>  
<5B01>;VBC ;;>?V4>3@5;C 7=878;0AL =0 46 % (45=L 1) B0 42 % (45=L 5) ?@8 >4=>G0A=>AC20==V  
;>?V4>3@5;C B0 ><5?@07>;C. 15@54=O 25;8G8=0 ?@83=VG5==O 03@530FVW B@><1>F8BV2 ?@8  
>4=>G0A=>AC20==V ;;>?V4>3@5;C B0 ><5?@07>;C 7<5=H8;0AO =0 47 % (G5@57 24 3>48=8) B0 30 %  
(45=L 5). □=H5 4>A;V465==O ?@>45<>=AB@C20;>; I> 70AB>AC20==O ;;>?V4>3@5;C B0 ><5?@07>;C  
2 @V7=89 G0A =5 CAC20;> WE 270T<>4VW, I>, 2V@>3V4=>, 7C<>2;5=> ?@83=VGC20;L=8< 2?;82<> >  
<5?@07>;C =0 CYP2C19. E>4V >1A5@20FV9=8E B0 ;V=VG=8E 4>A;V465=L >B@8<0=> AC?5@5G;82V  
40=V I>4> ;V=VG=8E ?@>O2V2 FVTW \$/\$270T<>4VW 7 B>G:8 7>@C 7=0G=8E A5@F52>-AC48==8E  
?>4V9.

52V4><89 <5E0=V7<

@8 70AB>AC20==V <5B>B@5:A0BC @07>< V7 9>3> @V2=V ?V428IC20;8AO C 45O:8E ?0FVT=BV2.  
>65 1CB8 ?>B@V1=5 B825 ?@8?8=5==O ?@89><C 57><5?@07>;C ?@8 70AB>AC20==V  
<5B>B@5:A0BC C 25;8:8E 4>70E.

?;82 V=H8E ;V:0@AL:8E 70A>1V2 =0 D0@<0:>:V=5B8:C 57><5?@07>;C  
7><5?@07>; <5B01>;V7CTBLAO CYP2C19 B0 CYP34. !C?CB=T ?5@>@0;L=5 70AB>AC20==O 57>  
<5?@07>;C B0 V=3V1VB>@C CYP34 ;:0@8B@>, ?@872>48;> 4> ?>42>T==O 5:A?>78FVW (AUC) 57>  
<5?@07>;C. !C?CB=T 70AB>AC20==O 57><5?@07>;C B0 :><1V=>20=>3> V=3V1VB>@C CYP2C19 B0  
CYP34 <>65 ?@872>48B8 4> 7@>AB0==O 5:A?>78FVW 57><5?@07>;C 1V;LH5 =V6 C42VGV.  
=3V1VB>@ CYP2C19 B0 CYP34 2>@8:>=07>; 71V;LHC202 AUCτ <5?@07>;C =0 280 %. >@5:FVO 4>78  
57><5?@07>;C =5 702648 ?>B@V1=0 2 B0:8E A8BC0FVOE. 4=0: 2>=0 <>65 1CB8 =5>1EV4=>N 4;0  
?0FVT=BV2 V7 BO6:8<8 ?>@CH5==O<8 DC=:FVW ?5GV=:8 B0 C 28?04:0E, :>;8 ?>:070=5  
4>23>B@820;5 ;V:C20==O.

@5?0@0B8, 740B=V AB8 >18420 FV D5@<5=B8 (B0:V O: @8D01V9), <>6CBL 7=86C20B8  
:>=F5=B@0FVW 57><5?@07>;C C A8@>20BFV :@>2V H;OE< ?>A8;5==O 9>3> <5B01>;V7

**A>I;82>ABV 70AB>AC20==O.**

# @07V 1C4L-O:8E B@82>6=8E A82;5==O 4V03=>7C.

"5@0?VO V=3V1VB>@0<8 ?@>B>==>W ?>65 45I> 71V;LHC20B8 @878: H;C=:>2>:-8H:>28E V=D5:FV9,  
B0:8E O: V=D5:FVW, 7C<>2;5=V *Salmonella* B0 *C0mpylobacter* (482. @>74V; «\$0@<0:>48=0  
5 @5:><5=4CTBLAO 70AB>A>2C20B8 57><5?@07>; >4=>G0A=> 7 0B070=02V@>< (482. @>74V; «70T  
<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9)). ./I> 70AB>AC20==O :>  
<1V=0FVW 0B070=02V@C 7 V=3V1VB>@0<8 ?@>B>==>W ?>1>2□O7:>28<, @5:><5=4CTBLAO ?8;L=>  
A?>AB5@V30B8 70 ?0FVT=B>< B0 ?V428I8B8 4>7C 0B070=02V@C 4> 400 <3 C ?>T4=0==V 7V 100 <3  
@8B>=02V@C; 4>7C 57><5?@07>;C 20 <3 ?5@528IC20B8 =5 A;V4.

7><5?@07>;, O: V 2AV ?@5?0@0B8, I> 1;>:CNBL A5:@5FVN :8A;>B8,<65 ?@83=VGC20B8 2A  
<:BC20==O 2VB0:>10;0: 3V?>- G8 0E;>@3V4@VW. &5 A;V4 <0B8 =0 C207V I>4> ?0FVT=BV2 7V  
7=865=8< 70?0A>< 2VB0@30=V7 D0:B>@0<8 @878:C ?>3V@H5=>3> 2A<:BC20==O 2VB0 12 ?@8  
4>23>B@820;V9 B5@0?VW.

7><5?@07>; V=3V1VB>@ CYP2C19. 0 ?>G0B:C B0 =0?@8:V=FV B5@0?VW 57<5?@07>;< A;V4  
2@0E>2C20B8 <6;82VABL 270T<>4VW V7 ?@5?0@0B0<8, I> <5B01>;V7CNBLAO CYP2C19. V47=0G5=  
> 270T<>4VN ?V4>3@5;5< B0 ><5?@07>;< (482. @>74V; <70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10  
<8 B0 V=HV 2848 270T<>4V9)). ;V=VG=0 7=0GCIVABL FVTW 270T<>4VW B>G=> =5 287=0G5=0. /:  
70?>1V6=89 70EV4 =5 @5:><5=4CTBLAO >4=>G0A=> 70AB>A>2C20B8 57<5?@07>; B0 ;>?V4>3@5;L.  
8?04:8 B06:>W 3V?><03=VTABV 28?04:V2 ?@>BO3<< @>:C. V?><03=VT728B>: <65 1CB8 ?>ABC?>28  
< B0 ;8H0B8AO =5?>ABV ?0FVT=BV2 V7 3V?><03=VTW B5@0?VW <03=VT< B0 ?@8?8=5==O  
70AB>AC20==O .

0FVT=B0<, 4;O O:8E ?5@5410G0TBLAO B@820;89 :C@A ;V:C20==O 01> O:V ?@89<0NBL V7 48  
3>:A8=>< G8 ?@5?0@0B0<8, 740B=8<8 A?@8G8=OB8 3V?><03=VT7 4VC@5B8:0<8), 4>FV;L=8< <65  
1CB8 28?@>BO3<< ;V:C20==O.

=3V1VB>@8 ?@>B>=>W ?>A>1;82> ?@8 70AB>AC20==V C 28A>:8E 4>70E B0 ?@>BO3<< B@820;>3>  
?5@V>4C (>1 @>:C), <>6CBL 45I? ?V428IC20B8 @878: ?5@5;> C ?0FVT=BV2 ;VB=L>3> 2V:C G8 7  
V=H8<8 D0:B>@0<8 @878:C. 57C;LB0B8 >3;04>28E 4>A;V465=L A2V4G0BL, I> V=3V1VB>@8  
?@>B>=>W ?>6CBL ?V428IC20B8 7030;L=89 @878: ?5@5;> %. 5O:>N N F5 ?V428I5==O <>65 1CB8 7C  
<2;5=> V=H8<8 D0:B>@0<8 @878:C. 0FVT=BV2, O:8< 703@>6CT @878: >AB5>?>@>7C, A;V4  
;V:C20B8 2V4?>2V4=> 4> 4VNG8E ;V=VG=8E :5@V2=8FB2; B0:>6 W< A;V4 >B@8 =0;56=C :V;L:VABL  
2VB0

?;82 =0 @57C;LB0B8 ;01>@0B>@=8E 0=0;V7V2  
V428I5=V @V2=V CgA <>6CBL 702060B8 4V03=>AB8FV =59@>5=4>:@8==8E ?CE;8=. )>1 FL>3>  
C=8:=CB8, A;V4 B82> ?@8?8=8B8 70AB>AC20==O 57><5?@07>;C I>=09<5=H5 70 ?OBL 4=V2 4> 28  
>65= D;0:>= <5=H5 1 <<>;L =0B@VN.

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

0=V I>4> 70AB>AC20==O 57><5?@07>;C 2 ?5@V>4 203VB=>ABV >1<565=V. >A;V465==O =0  
B20@8=0E =5 28O28;8 ?@O<>3> G8 >?>A5@54:>20=>3> H:V4;82>3> 2?;82C =0 5<1@V>D5B0;L=89  
@>728B>:. 0=V 4>A;V465=L @0F5W AC 157?>A5@54=V9 G8 >?>A5@54:>20=89 H:V4;8289 2?;82 =0  
203VB=VABL, ?>;>38 G8 ?VA;O?>;>3>289 @>728B>:. @87=0G0B8 5:AV< 203VB=8< 6V=:0< A;V4 7  
>15@56=VABN.

52V4><>, G8 ?@>=8:0T 57><5?@07>; C 3@C4=5 <>;>:. >A;V465=L 70 CG0ABN 6V=>:, O:V 3>4CNBL  
3@C44N, =5 ?@>2>48;>AO. ">

**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.**

0;>9<>2V@=>, I>1 5:AVC< 2?;8202 =0 740B=VABL :5@C20B8 02B>>1V;5< B0 ?@0FN20B8 7 V=H8<8  
<5E0=V7<0<8. V4 G0A ;V:C20==O ?@5?0@0B< <>6CBL A?>AB5@V30B8AL ?>1VG=V @50:FVW 7  
1>:C =5@2>2>W A8AB5<8 01> >@30=V2 7>@C.

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

>7C20==O

>@>A:V

=B8A5:@5B>@=0 B5@0?VO, C @07V, .:>;8 =5<>6;82> 70AB>A>2C20B8 ?5@>@0;L=89 H;OE  
22545==O 0FVT=B0<, O:V =5 <>6CBL ?@89<0B8 ;V:0@AL:89 70AV1 ?5@>@0;L=>, <>6=0 22>48B8  
?@5?0@0B ?0@5=B5@0;L=> C 4>7V 20-40 <3 >48= @07 =0 4>1C. >70 4;O ?0FVT=BV2 V7 @5D;N:A=8<  
57>D03VB>< AB0=>28BL 40 <3 >48= @07 =0 4>1C. >70 4;O ?0FVT=BV2, I> >45@6CNBL A8<0B8G=5  
;V:C20==O @5D;N:A=>W E2>@>18, AB0=>28BL 20 <3 >48= @07 =0 4>1C.

@8 ;V:C20==V 28@07>: H;C=:0, 7C<>2;5=8E 70AB>AC20==O< , 728G09=0 4>70 AB0=>28BL 20 <3 >48=  
@07 =0 4>1C. ;O 70?>1V30==O 28@07:0< H;C=:0 B0 420=04FOB8?0;>W :8H:8, 7C<>2;5=8< B5@0?VTN ,  
?0FVT=B0< 3@C?8 @878:C ?@87=0G0NBL ;V:0@AL:89 70AV1C 4>7V 20 <3 >48= @07 =0 4>1C.  
0728G09 ;V:C20==O 70 4>?><>3>N ;V:0@AL:>3> 70A>1C 4;O 2=CB@VH=L>25==>3> 22545==O T  
:>@>B:>B@820;8<, ?0FVT=BV2 A;V4 ?5@52>48B8 =0 ?5@>@0;L=5 70AB>AC20==O ;V:0@AL:>3>  
70A>1C O:><>30 H284H5.

>@>B:>B@820;5 ?V4B@8<0==O 35<>AB07C B0 ?@>DV;0:B8:0 ?>2B>@=>W :@>2>B5GV C  
?0FVT=BV2 ?VA;O 5=4>A:>?VG=>3> ;V:C20==O 3>AB@>W :@>2>B5GV 2=0A;V4>: 28@07:8 H;C=:0  
01> 420=04FOB8?0;>W :8H:8

VA;O B5@0?52B8G=>W 5=4>A:>?VW 3>AB@>W :@>2>B5GV 28@07>: H;C=:0 01> 420=04FOB8?0;>W  
:8H:8 22>4OBL 80 <3 ;V:0@AL:>3> 70A>1C C 283;O4V 1>;NA=>W V=DC7VW B@820;VABN 30 E28;8=,  
?VA;O G>3> ?@>4>26CNBL 22545==O ?@5?0@0BC C 283;O4V B@820;>W 2=CB@VH=L>25==>W  
V=DC7VW 7V H284:VABN 8 <3/3>48=C 2?@>4>26 3 4=V2 (72 3>48=).

VA;O ?0@5=B5@0;L=>3> ;V:C20==O B5@0?VNA;V4 ?@>4>268B8 70 4>?><>3>N ?5@>@0;L=8E  
70A>1V2, I> ?@83=VGCNBL :8A;>B=C A5:@5FVN.

!>AV1 70AB>AC20==O

=AB@C:FVW V7 ?@83>BC20==O 2V4=>2;5=>3> @>7G8=C =02545=V C 40=>74V;V =86G5 («  
=AB@C:FVW V7 70AB>AC20==O, 28:>@8AB0==O B0 CB8;V70FVW (C 2V4?>2V4=8E 28?04:0E)»).

=□T:FVW

>70 40 <3

5 <; 2V4=>2;5=>3> @>7G8=C (8 <3/<;) 22>4OBL C 283;O4V 2=CB@VH=L>25==>W V=T:FVW  
B@820;VABN I>=09<5=H5 3 E28;8=8.

>70 20 <3

2,5 <; 01> ?>;>28=C 2V4=>2;5=>3> @>7G8=C (8 <3/<;) 22>4OBL C 283;O4V 2=CB@VH=L>25==>W  
V=T:FVW B@820;VABN I>=09<5=H5 3 E28;8=8. 528:>@8AB0=89 @>7G8= CB8;V7CNBL.

=DC7VW

>70 40 <3

V4=>2;5=89 @>7G8= 22>4OBL C 283;O4V 2=CB@VH=L>25==>W V=DC7VW B@820;VABN10-30  
E28;8=.

>70 20 <3

>;>28=C 2V4=>2;5=>3> @>7G8=C 22>4OBL C 283;O4V 2=CB@VH=L>25==>W V=DC7VW  
B@820;VABN 10-30 E28;8=. 528:>@8AB0=89 @>7G8= CB8;V7CNBL.

>70 80 <3

V4=>2;5=89 @>7G8= 22>4OBL C 283;O4V B@820;>W 2=CB@VH=L>25==>W V=DC7VW ?@>BO3× 30  
E28;8=.

>70 8 <3/3>4

V4=>2;5=89 @>7G8= 22>4OBL C 283;O4V B@820;>W 2=CB@VH=L>25==>W V=DC7VW ?@>BO3×  
71,5 3>48=8 (@>7@0E>20=0 H284:VABL V=DC7VW 8<3/3>48=C; B5@ABV 2V4=>2;5=>3> @>7G8=C  
2:070=89 C @>74V;V «"5@ABV»).

>@CH5==O DC=:FVW =8@>:

;O ?0FVT=BV2 V7 ?>@CH5=O< DC=:FVW =8@>: :>@5:FVO 4>78 =5 T =5>1EV4=>N. A:V;L:8 4>A2V4  
70AB>AC20==O ?@5?0@0BC ?0FVT=B0< V7 BO6:>N =8@>:>2>N =54>AB0B=VABN >1<565=89, B0:8E  
?0FVT=BV2 A;V4 ;V:C20B8 7 >15@56=VABN (482. @>74V;«\$0@<0>:V=5B8:0»).

>@CH5==O DC=:FVW ?5GV=:8

%: ?0FVT=B0< V7 ;53:8<8 01> ?>0FVT=B0< V7 BO6:8<8 ?>@CH5==O<8 DC=:FVW ?5GV=:8 =5 A;V4  
?5@528IC20B8 <0:A8<0;L=C 4>7C 5:AVC<C 20 <3 (482. @>74V;«\$0@<0>:V=5B8:0»).

8@07:8, I> :@>2>B>G0BL: ?0FVT=B0< V7 ;53:8<8 01> ?>; ?0FVT=B0< V7 BO6:8<8 ?>@CH5==O<8 DC=:FVW ?5GV=:8 ?VA;O 22545==O ?>G0B:>2>W 1>;NA=>W 4>78 ?@5?0@0BC 5:AVG< 4;O V=DC7V9 80 <3 ?>40;LH5 22545==O ?@5?0@0BC C 283;O4V B@820;>W 2=CB@VH=L>25==>W V=DC7VW 7V H284:VABN 4<3/3>48=C ?@>BO3<> 71,5 3>48=8 <>65 1CB8 4>AB0B=V< (482. @>74V; «\$0@ <0:;>:V=5B8:0»).

0FVT=B8 ;VB=L>3> 2V:C  
>@5:FVO 4>78 =5 ?>B@V1=0.

VB8  
>7C20==O

VB8 2V:>< 1-18 @>:V2

/: 70AV1 4;O ?@83=VG5==O H;C=:>2>W A5:@5FVW C @07V, :>;8 ?5@>@0;L=89 ?@89>< ?@5?0@0BC =5<>6;8289

0FVT=B0<, O:V =5 <>6CBL ?@89<0B8 ?@5?0@0B ?5@>@0;L=>, 2 @04C ?>2=>3> ;V:C20==O % <>6=0 22>48B8 ?@5?0@0B ?0@5=B5@0;L=> >48= @07 =0 4>1C (4>78 2:070=V C B01;8FV =86G5).

0728G09 ;V:C20==O 70 4>?<>3>N ?@5?0@0BC 4;O 2=CB@VH=L>25==>3> 22545==O <0T B@820B8 =54>23> V ?0FVT=BV2 A;V4 ?5@52>48B8 =0 ?5@>@0;L=89 ?@89<> ;V:0@AL:>3> 70A>1C O:<>30 H284H5.

5:<>5=4>20=V 4>78 57<>5?@07>;C 4;O 2=C@VH=L>25==>3> 22545==O

V:>20 3@C?0	V:C20==O 5@>782=>3> @5D;N:A=>3> 57>D03VBC	!8<0B8G=5 ;V:C20==O %
1-11 @>:V2	0A0 BV;0 <20 :3: 10 <3 >48= @07 =0 4>1C 0A0 BV;0 ≥20 :3: 10 01> 20 <3 >48= @07 =0 4>1C	10 <3 >48= @07 =0 4>1C
12-18 @>:V2	40 <3 >48= @07 =0 4>1C	20 <3 >48= @07 =0 4>1C

!>AV1 70AB>AC20==O

=AB@C:FVW V7 ?@83>BC20==O 2V4=>2;5=>3> @>7G8=C =02545=V C 40=>74V;V =86G5 (« =AB@C:FVW V7 70AB>AC20==O, 28:>@8AB0==O B0 CB8;V70FVW (C 2V4?>2V4=8E 28?04:0E)»).

=□T:FVW

>70 40 <3

5 <; 2V4=>2;5=>3> @>7G8=C (8 <3/<;) 22>4OBL C 283;O4V 2=CB@VH=L>25==>W V=T:FVW B@820;VABN I>=09<5=H5 3 E28;8=8.

>70 20 <3

2,5 <; 01> ?>;>28=C 2V4=>2;5=>3> @>7G8=C (8 <3/<;) 22>4OBL C 283;O4V 2=CB@VH=L>25==>W V=T:FVW B@820;VABN I>=09<5=H5 3 E28;8=8. 528:>@8AB0=89 @>7G8= CB8;V7CNBL.

>70 10 <3

1,25 <; 2V4=>2;5=>3> @>7G8=C (8 <3/<;) 22>4OBL C 283;O4V 2=CB@VH=L>25==>W V=T:FVW B@820;VABN I>=09<5=H5 3 E28;8=8. 528:>@8AB0=89 @>7G8= CB8;V7CNBL.

=DC7VW

>70 40 <3

V4=>2;5=89 @>7G8= 22>4OBL C 283;O4V 2=CB@VH=L>25==>W V=DC7VW B@820;VABN10-30 E28;8=.

>70 20 <3

>;>28=C 2V4=>2;5=>3> @>7G8=C 22>4OBL C 283;O4V 2=CB@VH=L>25==>W V=DC7VW B@820;VABN 10-30 E28;8= 528:>@8AB0=89 @>7G8= CB8;V7CNBL.

>70 10 <3



'25@BL 2V4=>2;5=>3> @>7G8=C 22>4OBL C 283;O4V 2=CB@VH=L>25==>W V=DC7VW B@820;VABN 10-30 E28;8=. 528:>@8AB0=89 @>7G8= CB8;V7CNBL.

=AB@C:FVW V7 70AB>AC20==O, 28:>@8AB0==O B0 CB8;V70FVW (C 2V4?>2V4=8E 28?04:0E) 5@54 70AB>AC20==O< 2V4=>2;5=89 @>7G8= A;V4 2V7C0;L=> >3;O=CB8 =0 =0O2=VABL G0AB>: B0 7 @8AB>2C20B8 ;8H5 ?@>7>@89 @>7G8=. >7G8= ?@87=0G5=89 ;8H5 4;O >4=>@07>2>3> 70AB>AC20==O.

/:I> 25AL 2V4=>2;5=89 2=C =5 ?>B@V15=, =528:>@8AB0=89 @>7G8= A;V4 CB8;V7C20B8 2V4?>2V4=> 4>

>7G8= 4;O V=T:FV9 ?> 40 <3

>BCNBL @>7G8= 4;O V=T:FVW (8<3/<;), 4>40NG8 5 <; 0,9 % =0B@VN E;>@84C 4;O 2=CB@VH=L>25==>3> 70AB>AC20==O 4> D;0:>=C 57<<5?@07>;C 40 <3.

V4=>2;5=89 @>7G8= 4;O V=T:FV9 ?@>7>@89 B0 15710@2=89 01> B@>E8 6>2BC20B>3> :>;L>@C.

>7G8= 4;O V=DC7V9 ?> 40 <3

>BCNBL @>7G8= 4;O V=DC7V9, @>7G8=ONG8 24=>3> D;0:>=0 57<<5?@07>;C 40 <3 C 4> 100 <; 0,9 % E;>@84C =0B@VN 4;O 2=CB@VH=L>25==>3> 70AB>AC20==O.

>7G8= 4;O V=DC7V9 ?> 80 <3

>BCNBL @>7G8= 4;O V=DC7V9, @>7G8=ONG8 2E D;0:>=V2 57<<5?@07>;C ?> 40 <3 C 4> 100 <; 0,9 % E;>@84C =0B@VN 4;O 2=CB@VH=L>25==>3> 70AB>AC20==O.

V4=>2;5=89 @>7G8= 4;O V=DC7V9 ?@>7>@89 B0 15710@2=89 01> B@>E8 6>2BC20B>3> :>;L>@C.

### VB8.

0AB>A>2CNBL 4VBO< 2V:>< 2V4 1 @>:C O: 70AV1 4;O 0=B8A5:@5B>@=>W B5@0?VW C @07V, :>;8 ?5@>@0;L=89 ?@89>< ?@5?0@0BC =5<>6;8289.

### 5@54>7C20==O.

>A2V4 =02<8A=>3> ?5@54>7C20==O =0 40=89 G0A 4C65 >1<565=89. !8<0<8, I> 28=8:0;8 2=0A;V4>: ?5@>@0;L=>78 280 <3, 1C;8 ?@>O28 7 1>:C H;C=:>2>-.8H:>2>3> B@0:BC B0 A;01:VABL. 07>289 ?5@>@0;L=89 ?@89>< 80 <3 57<<5?@07>;C B0 2=CB@VH=L>25==5 22545==O 308 <3 57<<5?@07>;C ?@>BO3>< 24 3>48= =0A;V4:V2 =5 A?@8G8=O;8. !?5F8DVG=89 0=B84>B =52V4<<89. 7><5?@07>; 7=0G=8< G8=>< 72O7CTBLAO V7 1V;:0<8 ?;07<8 :@>2V V B>30=> 282>48BLAO 70 4>?><>3>N 4V0;V7C. /: V C 28?04:C 1C4L-O:>3> ?5@54>7C20==O, A;V4 =040B8 A8<0B8G=5 ;V:C20==O B0 268B8 7030;L=8E ?V4B@84V2.

### >IVG=V @50:FVW.

86G5=02545=V =51060=V @50:FVW =0 ?@5?0@0B 1C;8 28O2;5=V 01> ?V4>7@N20;8AO C ?@>3@0 A;V465=L 57<<5?@07>;C ?@8 9>3> ?5@>@0;L=>25==>AC20==V, 0 B0:>6 ?V4 G0A ?>AB <0@:5B8=3>2>3> A?>AB5@565==O 70 ?5@>@0;L=8< 70AB>AC20==O< ?@5?0@0BC. 50:FVW @>7?>4V;5=V 70 :0B53>@VO<8 70 G0AB>B>N: 4C65 G0AB> (>=1/10); G0AB> (>=1/100 - <1/10); =5G0AB> (>=1/1000 - <1/100); @V4:> (>=1/10000 - <1/1000); 4C65 @V4:> (<1/10000); =52V4<<0 G0AB>B0 (=5<>6;82> 287=0G8B8 70 =0O2=8<8 40=8<8).

>@CH5==O 7 I>:C :@>2V B0 ;VW A8AB5<8

V4:>: ;59:>?5=VO, B@><1>F8B>?5=VO.

C65 @V4:>: 03@0=C;>F8B>7, ?0=F8B>?5=VO.

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

V4:>: @50:FVW 3V?5@GCB;82>ABV, =0?@8::04, 30@OG:0, 0=3V>=52@>B8G=89 =01@O: B0 0=0DV;0:B8G=V @50:FVW/H>:.

>@CH5==O 7 I>:C <5B01>;V7

5G0AB>: ?5@8D5@8G=89 =01@O:.

V4:>: 3V?>=0B@VT.

52V4><0 G0AB>B0: 3V?><03=VT74V; «A>1;82>ABV 70AB>AC20==O»); BO6:0 3V?><03=VT

A8EVG=V @>7;048

5G0AB>: 157A>==O.

V4:>: 068B0FVO, A?;CB0=VABL A2V4>>ABV, 45?@5AVO.

C65 @V4:>: 03@5AVO, 30;NFV=0FVW.

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

'0AB>: 3>;>2=89 1V;L.

5G0AB>: 70?0<>@>G5==O, ?0@5AB57VO, A>=;82VABL

V4:>: ?>@CH5==O A<0:>28E 2V4GCBBV2.

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

5G0AB>: =5GVB:89 7V@.

>@CH5==O 7 I>:C >@30=V2 A;CEC B0 @V2=>2038

5G0AB>: 25@B83>.

>@CH5==O 7 I>:C >@30=V2 48E0==O, 3@C4=>W ;;VB:8 B0 A5@54>ABV==O

V4:>: 1@=>E>A?07<.

>@CH5==O 7 I>:C B@02=>W A8AB5<8

'0AB>: 1V;L C 682>BV, 70?>@, 4V0@5O,<5B5>@87<, =C4>B0/1;N20==O.

5G0AB>: ACEVABL C @>BV.

V4:>: AB><0B8B, H;C=:>2>-:8H:>289 :0=484>7.

52V4><0 G0AB>B0: A:>?VG=89 :>;VB.

>@CH5==O 7 I>:C 35?0B>1V;V0@=>W A8AB5<8

5G0AB>: 71V;LH5==O @V2=O ?5GV=:>28E D5@<5=BV2.

V4:>: 35?0B8B V7 6>2BO=8F5N G8 157 =5W.

C65 @V4:>: ?5GV=:>20 =54>AB0B=VABL, 5=F5D0;>?0BVO C ?0FVT=BV2 V7 ?>?5@54=L> =002=>N

E2>@>1>N ?5GV=:8.

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

'0AB>: @50:FVW C .

5G0AB>: 45@<0B8B, A25@1V6, 28A8?, :@>?82O=:0.

V4:>: 0;>?5FVO, D>B>GCB;82VABL.

C65 @V4:>: ?>;V<>@D=0 5@8B5<0, A8=4@> !BV25=A0-6>=A>=0, B>:A8G=89 5?V45@<0;L=89

=5:@>;V7.

>@CH5==O 7 I>:C A:5;5B=>W ;CG=>W B:0=8=8

5G0AB>: ?5@5;><8 AB53=0, 70?OABO 01> E@51B0 (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

V4:>: 0@B@0;3VO, .

C65 @V4:>: <O7>20 A;01:VABL

>@CH5==O 7 I>:C =8@>: B0 A5G>284V;L=>W A8AB5<8

C65 @V4:>: V=B5@AB8FV0;L=89 =5D@8B; C 45O:8E ?0FVT=BV2 ?>2V4><;O;>AO ?@> =8@:>2C

=54>AB0B=VABL

>@CH5==O 7 I>:C @5?@>4C:B82=>W A8AB5<8 B0 <>;>G=>W 70;>78

C65 @V4:>: 3V=5:><0ABVO.

030;L=V @>7;048 B0 @50:FVW C

V4:>: =574C60==O, ?>A8;5=5 ?>B>284V;5==O.

\* 50:FVW C AB5@V30;8AO ?5@5206=> C 4>A;V465==V V7 70AB>AC20==O< 28A>:8E 4>7 ?@>BO3<< 3 4V1 (72 3>48=). # ?@>3@0::V=VG=>3> 4>A;V465==O ?@5?0@0BC 57><5?@07>; 4;O 2=CB@VH=L>25==>3> 70AB>AC20==O =5 A?>AB5@V30;>AO ?>4@07=5==O AC48=, ?@>B5 1C;0 ?>W (=02.>;>25=>7=>W) V=T:FVW. 57C;LB0B8 4>;V=VG=>3> 4>A;V465==O 2:07C20;8 =0 B5, I> ::V=VG=5 ?@>O2;5==O ?>4@07=5==O B:0=8=8 1C;> ?>2O70=5 7 :=F5=B@0FVTN.

572>@>B=V ?>@CH5==O 7>@C 2V47=0G0;8AO C ?>>48=>:8E 28?04:0E C :@8B8G=> E2>@8E ?0FVT=BV2, O:V >B@8<5?@07>; (@0F5<0B) C 283;O4V 2=CB@VH=L>25==>W V=T:FVW, >A>1;82> C 28A>:8E 4>70E, >4=0: ?@8G8==>-0A;V4:>289 72O7>: =5 2AB0=>2;5=89.

54V0B@8G=0 ?>?C;OFVO

0=4>20=5, 2V4:@8B5, 4=5 4>A;V465==O 1C;> ?@>2545=> 7 <5B>N >FV=:8 D0@<0:>:V=5B8:8 1030B>@07>2>3> 2=CB@VH=L>25==>3> 70AB>AC20==O 57><5?@07>;C ?@>BO3<< 4 4=V2 ?@8 22545==V >48= @07 =0 4>1C C 4VB59 2V:< 2V4 0 4> 18 @>:V2 (482. @>74V; «\$0@<0:>:V=5B8:0»). AL>3> 4> >FV=:8 157?5:8 70A>1C 1C;> 70;CG5=> 57 ?0FVT=BV2 (8 4VB59 C 2V4V 1-5 @>:V2). 0=V 7 157?5:8 ?@5?0@0BC C73>46CNBLAO V7 2V4><8< ?@>DV;5< 157?5:8 57><5?@07>;C, V =>28E 703@>7 157?5FV ?0FVT=BV2 28O2;5=> =5 1C;>.

"5@ABV.2 @>:8.

"5@BC20==O @>7G8=C:

1C;0 ?@>45<>=AB@>20=0 EV 12 3>48= ?@8 30 !. B>G:8 7>@C 1V>;>3VW, ?@>4C:B A;V4 70AB>AC20B8 =5309=>.

#<>28 715@V30==O. 15@V30B8 2 =54>ABC?=>

5AC

0=89 ;V:0@AL:89 70AV1 =5 A;V4 70AB>A>2C20B8 7 V=H8<8 ;V:0@AL:8<8 70A>10<8, >:@V< 707=0G5=8E C @>74V;V «!>AV1 70AB>AC20==O B0 4>78».

#?0:>2:0. > 10 A::O=8E D;0:>=V2 7 ?>@>H:<< C :0@B>==V9 :>@>1FV.

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

8@>1=8:. AB@05=5:0 , (25FVO/AstraZeneca AB, Sweden.

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

\$>@A:0@30B0= 18 B0 5@BC=52535=, !>45@B0;T, 15185, (25FVO/ Forskargatan 18 och Gartunavagen, Sodertalje, 15185, Sweden.