

!" #&/

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

(CONCOR® !OR)

!;:04:

4VNG0 @5G>28=0: bisoprolol;

1 B01;5B:0 ?@>;>;C DC<0@0BC 2,5 <3;

4>?>28=8: :@5<=VN 4V>:A84 :>;>W4=89 1572>4=89; <03=VN AB50@0B;

:@>A?>2V4>=; F5;N;>70 :@8AB0;VG=0; :@>E<0;L :C:C@C47O=89; :0;LFVN

3V4@>D>AD0B 1572>4=89;

?;V2:>20 >I>;>=:0: 3V?@><5;>70 2910/15; <0:@>3>; 400; 48<5B8:>= 100; B8B0=C

4V>:A84 (171).

V:0@AL:0 D>@<0. "01;5B:8, 2:@8BV ?;V2:>2>N >1>;>=:>N.

A=>2=V DV78:>-EVABV: <0965 1V;>3> :>;L>@C, A5@F5?>4V1=V, 42>>?C::V

B01;5B:8, 2:@8BV ?;V2:>2>N >1>;>=:>N, 7 @8A:>N 7 >1>E 1>:V2.

\$0@<0:>B5@0?52B8G=0 3@C?0. !5;5:B82=V 1;>;:0B>@8 β-04@5=>@5F5?B>@V2.

>4 "% !0707.

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

\$0@<0:>48=0

VA>?@>;>; 28A>:>A5;5:B82=89 β<sub>1</sub>-04@5=>1;>;:0B>@. @8 70AB>AC20==V 2

B5@0?52B8G=8E 4>70E =5 <0T 2=CB@VH=L>W A8 28@065=8E <5<1@0=>-

AB01V;V7CNG8E 2;0AB82>AB59. '8=8BL 0=B80=3V=0;L=C B0 3V?>B5=782=C

4VN. <5=HCT ?>B@51C :0@40 2 :8A=V 7024O:8 7<5=H5==N !! V 7<5=H5==N

A5@F52>3> 28:84C B0 7=865==N 0@B5@V0;L=>3> B8A:C, 71V;LHCT

?>AB0G0==O :0@40 :8A=5< 70 @0EC=>: 7<5=H5==O :V=F52>-4V0AB>;VG=>3>

B8A:C V ?>4>265==O 4V0AB>;8. @5?0@0B <0T 4C65 =87L:C A?>@V4=5=VABL

V7 β<sub>2</sub>-@5F5?B>@0<8 3;04:>W =EV2 V AC48=, 0 B0:>6 V7 β<sub>2</sub>-@5F5?B>@0<8

5=4>:@8==>W A8AB5<8. @5?0@0B BV;L:8 C ?>>48=>:8E 28?04:0E <>65 2?;820B8

=0 3;04:C =EV2 V ?5@8D5@8G=8E 0@B5@V9, 0 B0:>6 =0 <5B01>;V7< 3;N:>78.

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

IA>@1FVO. V>4>ABC?=VABL AB0=>28BL 1;87L:> 90 %.

>7?>4V;. 1T< @>7?>4V;C AB0=>28BL 3,5 ;/:3. 2O7C20==O 7 1V;;0<8 ?;07<8 :@>2V

AB0=>28BL 1;87L:> 30 %.

5B01>;V7< B0 282545==O. VA>?@>;>; 282>48BLAO V7 >@30=V7<0 H;OE0<8:

50 % 1V>B@0=AD>@>@5==O <=50:B82=8E <5B01>;V BV2 B0

282>48BLAO =8@:0<8, 50 % 282>48BLAO =8@:0<8 C =57?@>;>;C AB0=>28BL 15

;/3>4. 024O:8 B@820;>4C =0?V2282545==O (10-12 3>48=) ?@5?0@0B 715@V30T

B5@0?52B8G=89 5D5:B 2?@>4>26 24 3>48= ?@8 70AB>AC20==V >48= @07 =0

4>1C.

V=V9=VABL. \$0@<0:>:V=5B8:0 1VA>?@>;>;C ;V=V9=0, WW ?>:07=8:8 =5

70;560BL 2V4 2V:C.

A>I;82V 3@C?8 ?0FVT=BV2. A:V;L:8 1VA>?@>;>; 282>48BLAO V7 >@30=V7  
@CH5==O< DC=:FV9 ?5GV=:8 01> ?>@CH5==O< DC=:FV9 =8@>: :>@5:FVO  
@5687C20==O =5 ?>B@V1=0. \$0@<0:;>:V=5B8:0 C ?0FVT=BV2 7V AB01V;L=>N  
E@>=VG=>N A5@F52>N =54>AB0B=VABN B0 7 ?>@CH5==O< DC=:FV9 ?5GV=:8  
01> =8@>: =5 282G0;0AO. # ?0FVT=BV2 V7 E@>=VG=>N A5@F52>N  
=54>AB0B=VABN DC=:FV>=0;L=>3> ;:0AC (70NYHA) @V25=L 1VA>?@>;>;C 2  
?:072V 28I5 B0 ?5@V>4 =0?V2282545==O ?@>;>=3>20=89 ?>@V2=O=> 7V  
74>@>28<8 4>1@>2>;LFO<8. 0:A8<0;L=0 :>=F5=B@0FVO C ?;07 :@>2V 2  
@V2=>206=> AB0=V AB0=>28BL 64+21 =3/<; ?@8 4>1>2V9 4>7V 10 <3 B0  
?5@V>4V =0?V2282545==O 17+5 3>48=.

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

>:070==O. V:C20==O E@>=VG=>W A5@F52>W =54>AB0B=>ABV 7  
A8AB>;VG=>N 48ADC=:FVTN ;V2>3> H;C=>G:0 2 :><1V=0FVW 7 V=3V1VB>@0  
<8 \$, 4VC@5B8:0<8, ?@8 =5>1EV4=>ABV A5@F528<8 3;V:>7840<8.

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

- □>AB@0 A5@F520 =54>AB0B=VABL 01> A5@F520 =54>AB0B=VABL C  
AB04VW 45:> ?>B@51CT 2=CB@VH=L>25==>W V=>B@>?=>W B5@0?VW;  
- :0@4V>35==89 H>;  
- 0B@V>25=B@8:C;O@=0 1;>:040 II V III ABC?5=O;  
- A8=4@< A;01:>ABV A8=CA>2>3> 2C7;0;  
- A8=>0B@V0;L=0 1;>:040;  
- A8<0B8G=0 1@048:0@4V0;  
- A8<0B8G=0 0@B5@V0;L=0 3V?>B5=7V0;  
- BO6:0 D>@<0 1@>=EV0;L=>W 0AB<8 01> BO6:89 ?5@51V3 E@>=VG=>3>  
>1AB@C:B82=>3> 70E2>@N20==O ;535=L;  
- BO6:0 D>@<0 >1;VB5@CNG8E 70E2>@N20=L ?5@8D5@8G=8E 0@B5@V9 01>  
E2>@>18 59=>;  
- D5>E@><>F8B><0, I> =5 ;V:C20;0AO;  
- <5B01>;VG=89 0F84>7;  
- ?V428I5=0 GCB;82VABL 4> 1VA>?@>;>;C 01> 4> V=H8E :>5=BV2 ?@5?0@0BC.

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

><1V=0FVW, O:V =5 @5:><5=4>20=> 70AB>A>2C20B8.  
- =B03>=VAB8 :0;LFDVN (3@C?8 25@0?0N 48;BV075@>GC20;L=C DC=:FVN  
:0@40 B0 0B@V>25=B@8:C;O@=C ?@>2V4=VABL. =CB@VH=L>25==5  
22545==O 25@0?0A>2CNBL β-1;>:0B>@8, <>65 ?@8725AB8 4> 28@065=>W  
3V?>B5=7VW B0 0B@V>25=B@8:C;O@=>W 1;>:048.  
- =B80@8B18 ;:0AC (=0?@8;:04, EV=V48=, 4V7?>V@0:0W=, D5=VB>W=,  
D;5:0W=V4, ?@>?0D5=>=): <>6;825 ?>B5=FDVN20==O 5D5:BC I>4>  
0B@V>25=B@8:C;O@=>W ?@>2V4=>ABV B0 ?>A8;5==O =530B82=>3>  
V=>B@>?=>3> 5D5:BC.  
- V?>B5=782=V ?@5?0@0B8 7 F5=B@0;L=8< <5E0=V7<>< 4VW (:;>=V48=,  
<5B8;4>?0, <.:A>=V48=, @8;<5=V48=): <>6;825 ?>3V@H5==O ?5@51V3C  
A5@F52>W =54>AB0B=>ABV 2=0A;V4>: 7=865==O F5=B@0;L=>3> A8>  
B>=CAC (7=865==O G0AB>B8 A5@F528E A:>@>G5=L V A5@F52>3> 28:84C,  
207>48;0B0FVO).  
0?B>20 2V4A>1;82> O:I> 9>:0B>@V2 β-04@5=>@5F5?B>@V2, <>65  
?V428I8B8 @878: 28=8=:5==O @8:>H5B=>W 3V?5@B5=7VW.  
><1V=0FVW, O:V A;V4 70AB>A>2C20B8 7 >15@56=VABN  
- =B03>=VAB8 :0;LFDVN 483V4@>?V@848=>2>3> @O4C (=0?@8;:04, D5;>48?V=, 0  
<:>48?V=): <>6;825 ?V428I5==O @878:C 28=8=:5==O 0@B5@V0;L=>W  
3V?>B5=7VW. 5 28;:NG0TBLAO <>6;82VABL 7@>AB0==O =530B82=>3> ??:82C  
=0 V=>B@>?=>C DC=:FVN :0@40 C ?0FVT=BV2 V7 A5@F52>N =54>AB0B=VABN.

- =B80@8B40@>=): <>6;825 ?>B5= FVN20==O 2?;82C =0 0B@V>25=B@8:C;O@=C ?@>2V4=VABL.

- B-1;>:0B>@8W 4VW (=0?@8:;04, I> G=8E :@0?;OE 4;O ;V:C20==O 3;0C:<>8): <>6;825 ?V4A8;5==O A8AB5<=8E 5D5:BV2 1VA>?@>;>;C.

- 0@0A8

- =AC;V= B0 ?5@>@0;L=V 3V?>3;V:518: ?V4A8;5==O 3V?>3;V:5W 4VW. ;>:040 B-04@5=>@5F5?B>@V2 <>65 <0A:C20B8 A8<8 3V?>3;V:5

- 0A>18 4;O 0=5AB57VW: >A;01;5==O @5D;5:B>@=>W B0EV:0@4VW B0 ?V428I5==O @878:C 0@B5@V0;L=>W 3V?>B5=7VW.

- !5@F52V 3;V:>7848: 7=865==O G0AB>B8 A5@F528E A:>@>G5=L, 71V;LH5==O G0AC 0B@V>25=B@8:C;O@=>W ?@>2V4=>ABV.

- 5AB5@>W4=V ?@>B870?0;L=V 70A>18 (): <>6;825 ?>A;01;5==O 3V?>B5=782=>3> 5D5:BC 1VA>?@>;>;C.

- B-A8

- !8W :C;L302>ABV. >4V1=0 270T<>4VO 2V@>3V4=VH0 ?@8 70AB>AC20==V =5A5;5:B82=8E B-1;>:0B>@V2.

@8 ACAC20==V 7 0=B83V?5@B5=782=8<8 70A>10<8 B0 70A>10<8, I> <0NBL 3V?>B5=782=C 4VN (=0?@8:;04, B@8F8:;VG=V 0=B845?@5A0=B8, 10@1VBC@0B8, D5=>BV078=), <>6;825 ?V428I5==O @878:C 0@B5@V0;L=>W 3V?>B5=7VW.

><1V=0FVW, I> <>6;82V.

- 5D;>EV=: <>6;825 ?V428I5==O @878:C @>728B:C 1@048:0@4VW.

- =3V1VB>@8 (70 28=OB:>< V=3V1VB>@V2 B8?C ): ?V428I5==O 3V?>B5=782=>3> 5D5:BC B-1;>:0B>@V2, 0;5 T @878: @>728B:C 3V?5@B>=VG=>3> :@87C.

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

V:C20==O AB01V;L=>W E@>=VG=>W A5@F52>W =54>AB0B=>ABV V7 70AB>AC20==O< 1VA>?@>;>;C A;V4 @>?>G8=0B8 7 D078 B8B@C20==O.

0FVT=B0< 7 VH5N E2>@>1>N A5@FO ;V:C20==O =5 A;V4 ?@8?8=OB8 @0?B>2> 157 :@09=L>W =5>1EV4=>ABV, B>F5 <>65 ?@8725AB8 4> B@0=78B>@=>3> ?>3V@H5==O AB0=C. =VFN20==O B0 ?@8?8=5==O ;V:C20==O 1VA>?@>;>;< 28<030T @53C;O@=>3> <=>VB>@8=3C.

0 40=89 G0A =5<0T 4>AB0B=L>3> B5@0?52B8G=>3> 4>A2V4C ;V:C20==O E@>=VG=>W A5@F52>W =54>AB0B=>ABV C ?0FVT=BV2 V7 =0ABC?=8<8

70E2>@N20==O<8 V ?0B>;>3VG=8<8 AB0=0<8: FC:@>289 4V015B B8?C, BO6:V ?>@CH5==O DC=:FV9 =8@>., BO6:V ?>@CH5==O DC=:FV9 ?5GV=:8,

@5AB@8:B82=0 :0@4V>?0BVO, 2@>465=V 2048 A5@FO, 35<>48=0 7=0GCIV ;:0?0==V 2048 A5@FO, V=D0@:B :0@40 ?@>BO3<< >AB0==VE 3

@5?0@0B A;V4 70AB>A>2C20B8 7 >15@56=VABN ?0FVT=B0< ?@8 B0:8E AB0=0E:

- 1@>=E>A?07< (?@8 1@>=EV0;L=V9 0AB1AB@C:B82=8E 70E2>@N20==OE 48E0;L=8E H;OEV2);

- FC:@>289 4V015B 7V 7=0G=8<8 :>;820==O<8 @V2=O 3;N:>78 2 :@>2V; A8<8 3V?>3;V:5

- AC2>@0 4VTB0;

- ?@>2545==O 45A5=A81V;V70FV9=>W B5@0?VW./: V V=HV B-1;>:0B>@8, 1VA>?@>;>;<>65 ?V4A8;N20B8 GCB;82VABL 4> 0;5@35=V2 B0 71V;LHC20B8

206:VABL 0=0DV;0:B8G=8E @50:FV9. # B0:8E 28?04:0E ;V:C20==O 04@5=0;V=< =5 702648 40T ?>78B82=89 B5@0?52B8G=89 5D5:B;

- 0B@V>25=B@8:C;O@=0 1;>:040 I ABC?5=O;

- AB5=>:0@4VO @8=F<5B0;0;

- >1;VB5@CNGV 70E2>@N20==O ?5@8D5@8G=8E 0@B5@V9 (=0 ?>G0B:C B5@0?VW <>6;825 ?>A8;5==O A:0@3);

- 7030;L=0 0=5AB57VO.

5>1EV4=> >1>2O7:>2> ?>?5@548B8 ;V:0@O-0=5AB57V>;>30 ?@>  
70AB>AC20==O 1;>:0B>@V2 β-04@5=>@5F5?B>@V2. # ?0FVT=BV2, O:8  
< ?;0=CTBLAO 7030;L=0 0=5AB57VO, 70AB>AC20==O β-1;>:0B>@V2  
7=86CT 28?04:8 0@8B:0@40 2?@>4>26 22545==O 2 =0@:>7, V=BC10FVW B0  
?VA;O>?5@0FV9=>3> ?5@V>4C. 5:×5=4>20=> ?@>4>26C20B8 70AB>AC20==O  
15B0-1;>:0B>@V2 ?V4 G0A ?5@8>?5@0FV9=>3> ?5@V>4C. =5AB57V>;>3  
?>28=5= 2@0E>2C20B8 ?>B5= FV9=C 270T<>4VN 7 V=H8<8 ;V:0<8, O:0 <>65  
?@8725AB8 4> 1@04V0@8B@=>W B0EV:0@4VW B0 7=865==O <>6;82>AB59  
@5D;5:B>@=>3> <5E0=V72>2B@0B8. # @07V 2V4?@>;>;C ?5@54 >?5@0B82=8  
<8 2B@CG0==O<8 4>7C A;V4 ?>ABC?>2> 7=878B8 B0 ?@8?8=8B8  
70AB>AC20==O ?@5?0@0BC 70 48 3>48= 4> 7030;L=>W 0=5AB57VW.  
><1V=0FVW 1VA>?@>;>;C 7 0=B03>=VAB0<8 :0;L;FVN 3@C?8 25@0?0 48;BV075  
@8 1@>=EV0;L=V9 0AB V=H8E E@>=VG=8E >1AB@C:B82=8E  
70E2>@N20==OE ;535=L ?>:070=0 AC?CB=O B5@0?VO 1@>=E>48;0B0B>@0<8. #  
45O:8E 28?04:0E =0 B;V ?@89>=EV0;L=>N 0AB<>N G5@57 ?V428I5==O  
@578AB5=B=>ABV 48E0;L=8E H;OE2 <>6CBL ?>B@51C20B8 1V;LH 28A>:8E  
4>7 β-A8  
%2>@8<=0 ?A>@V07 (C B.G. 2 0=0<=57V) β-1;>:0B>@8 ?@87=0G0NBL ?VA;O  
@5B5;L=>3> A?V22V4=>H5==O :>@8ABL/@878:.  
0FVT=B0< V7 D5>E@><>F8B><>N ?@87=0G0NBL 1VA>?@>;>; BV;L:8 ?VA;O  
?@87=0G5==O B5@0?VW α-04@5=>1;>:0B>@0<8.  
!8<8 B8@5>B>:A8:>7C <>6CBL 1CB8 70<0A:>20=V =0 B;V 70AB>AC20==O  
1VA>?@>;>;C.

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

03VB=VABL VA>?@>;>; <0T D0@<0:>;>3VG=V 2;0AB82>ABV, O:V <>6CBL  
A?@8G8=8B8 H:V4;8289 2?;82 =0 ?5@51V3 203VB=>ABV B0/01> @>728B>: ?;>40  
/=>2>=0@>465=>3>. /: ?@028;>, β-04@5=>1;>:0B>@8 7=5=HCNBL ?;0F5=B0@=89  
:@>2>BV:, I> <>65 A?@8G8=OB8 70B@8 2=CB@VH=L>CB@>1=>3> @>728B:C,  
2=CB@VH=L>CB@>1=C A<5@BL, <8<>2V;L=89 01>@B 01> ?5@54G0A=V ?>;>38  
. >6CBL @>728=CB8AO ?>1VG=V 5D5:B8 C ?;>40 B0 =>2>=0@>465=>3>  
(=0?@8:;04, 3V?>3;V:5/:I> ;V:C20==O β-1;>:0B>@0<8 =5>1EV4=5, 1060=>, I>1 F5  
1C2 β<sub>1</sub>-A5;5:B82=89 04@5=>1;>:0B>@.  
# ?5@V>4 203VB=>ABV ?@5?0@0B 70AB>A>2CNBL BV;L:8 B>4V, :>;8  
>GV:C20=0 :>@8ABL 4;O <0B5@V ?5@528ICT ?>B5= FV9=89 @878: 4;O ?;>40.  
5>1EV4=> :>=B@>;N20B8 <0B:>2>?;0F5=B0@=89 :@>2>BV: B0 7@>AB0==O  
?;>40. # @07V H:V4;82>3> 2?;82C =0 ?5@51V3 203VB=>ABV 01> ?;V4 A;V4  
@>73;O=CB8 <>6;82VABL0;LB5@=0B82=>3> ;V:C20==O.  
VA;O ?>;>3V2 =>2>=0@>465=89<0T 7=0E>48B8AO ?V4 @5B5;L=8< =03;O4>  
5@V>4 3>4C20==O 3@C44N. 0=8E I>4> 5:A:@5FVW 1VA>?@>;>;C C 3@C4=5  
<>;>: >=5<0T, B<5=4CTBLAO 70AB>A>2C20B8 1VA>?@>;>; ?V4 G0A  
3>4C20==O 3@C44N.

**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.**  
# E>4V 4>A;V465=L ?0FVT=BV2 7 VH5N E2>@>1>N A5@FO ?@5?0@0B =5  
2?;8202 =0 740B=VABL :5@C20B8 02B>>1V;5  
>:@5<8E 28?04:0E ?@5?0@0B <>65 2?;8=CB8 =0 740B=VABL :5@C20B8  
02B>B@0=A?>@B>< 01> ?@0FN20B8 7V A:;04=8<8 <5E0=V7<0<8. A>1;82C  
C203C =5>1EV4=> ?@84V;OB8 =0 ?>G0B:C ;V:C20==O, ?@8 778 ?@5?0@0BC 01>  
?@8 270T<>4VW 7 0;>3>;5<.

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

@5?0@0B >=>@ >@ A;V4 ?@89<0B8, =5 @>76>2CNG8, 2@0=FV ?V4 G0A  
A=V40=:C, 70?820NG8 =525;8:>N :V;L:VABN @V48=8.

!B0=40@B=0 B5@0?VO E@>=VG=>W A5@F52>W =54>AB0B=>ABV:  
V=3V1VB>@8 \$ 01> 0=B03>=VAB8 0=3V>B5=78=C , 1;>:0B>@8 β -  
04@5=>@5F5?B>@V2, 4VC@5B8:8 V, C @07V =5>1EV4=>ABV, A5@F52V  
3;V:>7848.

0 ?>G0B>: ;V:C20==O 1VA>?@>;>;< ?0FVT=B =5 ?>28=5= <0B8 >7=0:  
703>AB@5==O. >6;825 B@0=78B>@=5 ?>3V@H5==O A5@F52>W  
=54>AB0B=>ABV, 0@B5@V0;L=0 3V?>B5=7VO 01> 1@048:0@4VO ?@>B03<  
?5@V>4C B8B@C20==O B0 ?VA;O =L>3>.

5@V>4 B8B@C20==O 4>78.

V:C20==O E@>=VG=>W A5@F52>W =54>AB0B=>ABV 1VA>?@>;>;<  
@>?>G8=0TBLAO 2V4?>2V4=> 4> =0ABC?=>W AE5<8 B8B@C20==O B0 <>65  
:>@83C20B8AO 70;56=> 2V4 V=482V4C0;L=8E @50:FV9 >@30=V7  
1,25 <3 1VA>?@>;>;C DC<0@0BC 1 @07 =0 4>1C 2?@>4>26 1 B86=O, O:I> 4>1@5  
?5@5=>A8BLAO, ?V428I8B8 4>

2,5 <3 1VA>?@>;>;C DC<0@0BC 1 @07 =0 4>1C 2?@>4>26 =0ABC?=>3> 1 B86=O,  
O:I> 4>1@5 ?5@5=>A8BLAO, ?V428I8B8 4>

3,75 <3 1VA>?@>;>;C DC<0@0BC 1 @07 =0 4>1C 2?@>4>26 =0ABC?=>3> 1  
B86=O, O:I> 4>1@5 ?5@5=>A8BLAO, ?V428I8B8 4>

5 <3 1VA>?@>;>;C DC<0@0BC 1 @07 =0 4>1C 2?@>4>26 =0ABC?=8E 4 B86=V2,  
O:I> 4>1@5 ?5@5=>A8BLAO, ?V428I8B8 4>

7,5 <3 1VA>?@>;>;C DC<0@0BC 1 @07 =0 4>1C 2?@>4>26 =0ABC?=8E 4 B86=V2,  
O:I> 4>1@5 ?5@5=>A8BLAO, ?V428I8B8 4>

10 <3 1VA>?@>;>;C DC<0@0BC 1 @07 =0 4>1C O: ?V4B@8

0:A8<0;L=0 @5:><5=4>20=0 4>70 1VA>?@>;>;C DC<0@0BC AB0=>28BL 10 <3 1  
@07 =0 4>1C.

V4 G0A ?5@V>4C B8B@C20==O =5>1EV4=89 @5B5;L=89 =03;O4 70 ?>:07=8:0<8  
68BBT4VO;L=>ABV (0@B5@V0;L=89 B8A.; G0AB>B0 A5@F528E A:>@>G5=L) V  
A8<0<8 ?@>3@5AC20==O A5@F52>W =54>AB0B=>ABV. !8<8 <>6CBL  
@>72820B8AO 7 ?5@H>3> 4=O ?VA;O ?>G0B:C ;V:C20==O.

>48DV:0FVO ;V:C20==O.

/:I> <0:A8<0;L=0 @5:><5=4>20=0 4>70 ?>30=> ?5@5=>A8BLAO, <>6;825

?>ABC?>25 7=865==O 4>78. /:I> ?V4 G0A ?5@V>4C B8B@C20==O 01> ?VA;O

=5W A?>AB5@V30TBLAO ?>3V@H5==O A5@F52>W =54>AB0B=>ABV,

@>72820TBLAO 0@B5@V0;L=0 3V?>B5=7VO 01> 1@048:0@4VO, @5:>

<5=4CTBLAO 2V4:>@83C20B8 4>7C20==O ?@5?0@0BC, I> <>65 ?>B@51C20B8

B82>3> 7=865==O 4>7C20==O 1VA>?@>;>;C 01> ?@87C?8=5==O ;V:C20==O.

VA;O AB01V;V70FVW AB0=C ?0FVT=B0 702648 A;V4 @>73;O40B8<>6;82VABL

?>2B>@=>W V=VVF0FVW ;V:C20==O 1VA>?@>;>;>

C@A ;V:C20==O AB01V;L=>W E@>=VG=>W A5@F52>W =54>AB0B=>ABV

1VA>?@>;>;< T B@820;8

5 A;V4 ?@8?8=OB8 ;V:C20==O @0?B>2> B0 7<5=4>20=5 4>7C20==O 157

:>=AC;LB0FVW 7 ;V:0@5<, >A:V;L:8 F5 <>65 ?@8725AB8 4> ?>3V@H5==O

AB0=C ?0FVT=B0. # @07V =5>1EV4=>ABV ;V:C20==O ?@5?0@0B< A;V4

7025@HC20B8 ?>2V;L=>, ?>ABC?>2> 7=86CNG8 4>7C.

0FVT=B8 7 ?>@CH5==O<8 DC=:FV9 ?5GV=:8 0I> =8@>:.

5<0T 40=8E I>4> D0@<0>:V=5B8:8 1VA>?@>;>;C C ?0FVT=BV2 V7 E@>=VG=>N

A5@F52>N =54>AB0B=VABN >4=>G0A=> 7 ?>@CH5==O<8 DC=:FV9 ?5GV=:8

01> =8@>:, B>7C =5>1EV4=> 7 >A>1;82>N >15@56=VABN.

0FVT=B8 ;VB=L>3> 2V:C=5 ?>B@51CNBL :>@83C20==O 4>78.

**VB8.** ;V=VG=V 40=V I>4> 5D5:B82=>ABV V 157?5:8 70AB>AC20==O

?@5?0@0BC 4;O ;V:C20==O 4VB59 2V4ACB=V, B?@>;>; =5 @5:><5=4CTBLAO

70AB>A>2C20B8 2 ?54V0B@8G=V9 ?@0:B8FV.

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

@8 ?5@54>7C20==V (=0?@8:;04, 70AB>AC20==O 4>1>2>W 4>78 15 <3 70  
09G0ABVH8<8 >7=0:0<8 ?5@54>7C20==O B -1;:>0B>@0<8 T 1@048:0@4VO,  
0@B5@V0;L=0 3V?>B5=7VO, 3>AB@0 A5@F520 =54>AB0B=VABL, 3V?>3;V:5  
=E>A?070 40=89 G0A 2V4><> 45:V;L:0 28?04:V2 ?5@54>7C20==O (<0:A8<0;L=0  
4>70 2000 <3) 1VA>?@>;>;C. V40@B5@V0;L=0 3V?>B5=7VO. #AV ?0FVT=B8  
>4C60;8. A=CT H8@>:0 20@V015;L=VABL V=482V4C0;L=>W GCB;82>ABV 4>  
>4=>:@0B=>W 28A>:>W 4>78 1VA>?@>;>;C, ?0FVT=B8 7 A5@F52>N  
=54>AB0B=VABN<>6CBL 1CB8 1V;LH GCB;82V 4> ?@5?0@0BC. ">?>G8=0B8 7  
?>ABC?>28< 71V;LH5==O< 4>7C20==O (482. @>74V; <!>AV1 70AB>AC20==O B0  
4>78»).

# 28?04:C ?5@54>7C20==O =5>1EV4=> =5309=> 725@=CB8AO 4> ;V:0@O.  
@8 ?5@54>7C20==V ?@8?8=ONBL ;V:C20==O ?@5?0@0B< B0 ?@>2>4OBL  
?V4B@8

@8 1@048:0@4VW: 2=CB@VH=L>25==5 22545==O 0B@>?V=C. /:I> @50:FVO  
2V4ACB=O, 7 >15@56=VABN 22>48B8 V7>?@5=0;V= 01> V=H89 ?@5?0@0B 7  
?>78B82=8< E@>=>B@>?>8< 5D5:B>28E 28?04:0E <>65 7=04>18B8AL  
B@0=A25=>7=5 22545==O HBCG=>3> 2>4VO @8B

@8 0@B5@V0;L=V9 3V?>B5=7VW: 2=CB@VH=L>25==5 22545==O @V48=8 B0  
AC48=>72C6C20;L=8E ?@5?0@0BV2. =CB@VH=L>25==5 22545==O 3;N:03>=C  
<>65 1CB8 :>@8A=8

@8 0B@V>25=B@8:C;O@=V9 1;:>:04V II V III ABC?5=O: @5B5;L=5  
A?>AB5@565==O B0 V=DC7V9=5 22545==O V7?>@5=0;V=C 01> B@0=A25=>7=5  
22545==O :0@4V>AB8@0.

@8 703>AB@5==V E@>=VG=>W A5@F52>W =54>AB0B=>ABV:  
2=CB@VH=L>25==5 22545==O 4VC@5B8G=8E 70A>1V2, V=>B@>?=8E  
?@5?0@0BV2, 207>48;0B0B>@V2.

@8 1@>=E>A?07=E>;VB8G=V ?@5?0@0B8 (=0?@8:;04, V7?>@5=0;V=), B2-  
04@5=>DV;V=.

@8 3V?>3;V:525==5 22545==O 3;N:>78.

### >1VG=V @50:FVW.

51060=V 5D5:B8 70 G0AB>B>N 28=8:=5==O ;:0A8DV:CNBL 70 B0:8<8 :0B53>@VO  
<8:

4C65 G0AB> ( $\geq 1/10$ ), G0AB> ( $\geq 1/100$  V < 1/10), =5G0AB> ( $\geq 1/1000$  V < 1/100),  
@V4:> ( $\geq 1/10000$  V < 1/1000), 4C65 @V4:> (< 1/10000).

I>:C A5@F52>-AC48==>W A8AB5<8.

C65 G0AB>: 1@048:0@4VO.

'0AB>: ?>3V@H5==O A5@F52>W =54>AB0B=>ABV, 2V4GCBBO E>;>4C 01> >=V  
:, 0@B5@V0;L=0 3V?>B5=7VO.

5G0AB>: ?>@CH5==O 0B@V>25=B@8:C;O@=>W ?@>2V4=>ABV,  
>@B>AB0B8G=0 3V?>B5=7VO.

I>:C =5@2>2>W A8AB5<8.

'0AB>: 70?0<>@>G5==O, 3>;>2=89 1V;L.

V4:>: =5?@8B><=VABL.

I>:C >@30=V2 7>@C.

V4:>: 7=865==O A;L>7>284V;5==O (B@510 2@0E>2C20B8 ?@8 =>AV==V  
:>=B0:B=8E ;V=7).

C65 @V4:>: :>=N=:B82VB.

I>:C >@30=V2 A;CEC.

V4:>: ?>3V@H5==O A;CEC.

I>:C 48E0;L=>W A8AB5<8.

5G0AB>: 1@>=E>A?07< C ?0FVT=BV2 V7 1@>=EV0;L=>N 0AB<>N 01>  
>1AB@C:B82=8<8 70E2>@N20==O<8 48E0;L=8E H;OEV2 2 0=0<=57V.

V4:>: 0;5@3VG=89 @8=VB.

I>:C B@02=>3> B@0:BC.

'0AB>: =C4>B0, 1;N20==O, 4V0@5O, 70?>@.

I>:C H:V@8.

V4:>: @50:FVW 3V?5@GCB;82>ABV (A25@1V6, ?>G5@2>=V==O, 28A8?0==O).

C65 @V4:>: 0;>?5FVO. @8 ;V:C20==V B-1;>:0B>@08 <>65 A?>AB5@V30B8AO

?>3V@H5==O AB0=C E2>@8E =0 ?A>@V07 C 283;O4V ?A>@V0B8G=>3>

28A8?0==O.

I>:C :VAB:>2>-<□O7>2>W A8AB5<8.

5G0AB>: <O7>20 A;01:VABL, AC4<8.

I>:C ?5GV=:8.

V4:>: 35?0B8B.

I>:C @5?@>4C:B82=>W A8AB5<8.

V4:>: ?>@CH5==O ?>B5=FWW.

A8EVG=V @>7;048.

5G0AB>: 45?@5AVO, ?>@CH5==O A=C.

V4:>: =VG=V :>H<0@8, 30;NF8=0FVW.

01>@0B>@=V ?>:07=8:8.

V4:>: ?V428I5==O @V2=O B@83;VF5@84V2 C :@>2V, ?V428I5==O 0:B82=>ABV

?5GV=:>28E D5@<5=BV2 C ?;072V (!", ").

030;L=V @>7;048.

'0AB>: 0AB5=VO, 2B><;N20=VABL.

"5@ABV.3 @>:8.

#<>28 715@V30==O. 15@V30B8 2 >@83V=0;L=V9 C?0:>2FV ?@8 B5ABC?=>

#?0:>2:0.> 10 B01;5B>: C 1;VAB5@V; ?> 3 1;VAB5@8 2 :0@B>==V9 :>@>1FV.

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

8@>1=8:. 5@: 0, V<5GG8=0/Merck KGaA, Germany.

VAF57=0E>465==O 28@>1=8:0 B0 9>3> 04@5A020465==O 4VO;L=>ABV.

\$@0=:DC@B5@ (B@0AA5 250, 64293 0@Frankfurter Strasse 250, 64293 Darmstadt,

Germany.