

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

!□ \$□ ,□
(SALOFALK®)

!;:04:

4VNG0 @5G>28=0: <5A0;078=
1 B01;5B:0, 2:@8B0 >1>;>=:>N, :8H:>2>@>7G8==0, (5-0A0;VF8;>2>W :8A;>B8);
4>?>28=8: =0B@VN :0@1>=0B 1572>4=89, 3;VF8=, ?>2V4>= (□25), F5;N;>70 :@8AB0;VG=0, :@5<=VN
4V>:A84 :>;>W4=89 1572>4=89, :0;LFVN AB50@0B, 3V?@<<5;>70, <5B0:@8;0B=89 A>?>;V<5@ (B8?),
B0;L:, B8B0=C 4V>:A84 (171), 70;V70 3V4@>:A84 6>2B89 (172), <0:@>3>; 6000, 0:@8;0B=89 A>?>;V
<5@.

1 B01;5B:0, 2:@8B0 >1>;>=:>N, :8H:>2>@>7G8==0, 500 <3 <5A0;078=C (5-0A0;VF8;>2>W :8A;>B8);
4>?>28=8: =0B@VN :0@1>=0B 1572>4=89, 3;VF8=, ?>2V4>= (25), F5;N;>70 :@8AB0;VG=0, :@5<=VN
4V>:A84 :>;>W4=89 1572>4=89, :0;LFVN AB50@0B, :@>A:0@<5;>70 =0B@VN, 3V?@<<5;>70,
<5B0:@8;0B=89 A>?>;V<5@ (B8?), B0;L:, B8B0=C 4V>:A84 (171), 70;V70 3V4@>:A84 6>2B89 (172),
<0:@>3>; 6000, 0:@8;0B=89 A>?>;V<5@.

V:0@AL:0 D>@<0. "01;5B:8, 2:@8BV >1>;>=:>N, :8H:>2>@>7G8==V.

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

250 <3: 2V4 <0A;O=>-6>2B>3> 4> >E@O=>3> :>;L>@C, 3;045=L:V, :@C3;V B01;5B:8 7
=52V4?>;V@>20=>N ?>25@E=5N.

500 <3: 2V4 <0A;O=>-6>2B>3> 4> >E@O=>3> :>;L>@C, =53;O=F52V B01;5B:8, ?@>4>23C20B>W D>@
<8, 7 3;045=L:>N ?>25@E=5N 157 ?>

\$0@<0:>B5@0?52B8G=0 3@C?0. @>B870?0;L=V 70A>18, I> 70AB>A>2CNBLAO 4;O ;V:C20==O
70E2>@N20=L :8H5G=8:C. >4 "X 07!02.

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

\$0@<0:>48=0

5E0=V7< ?@>B870?0;L=>W 4VW =52V4<<89. 57C;LB0B8 4>A;V465=L in vitro A2V4G0BL, I> ?52=C
@>;L <>65 <0B8 V=3V1C20==O ;V?>>:A835=078.

C;> B0:>6 ?@>45<>=AB@>20=> 2?;82 =0 :>=F5=B@0FVN ?@>AB03;0=48=V2 C A;87>2V9 >1>;>=FV
:8H5G=8:C.

5A0;078= (5-0A0;VF8;>20 :8A;>B0/5-!) <>65 72 O7C20B8 2V;L=V @048:0;8.

5A0;078= ?@8 ?5@>@0;L=>2V, B0:8< G8=><, =5 T ACBBT28<8 4;O B5@0?52B8G=>3> 5D5:BC, 0

A:>@VH5 O2;ONBLAO D0:B>@<< =5H:V4;82>ABV. "01;5B:8 !0;>D0;L:C T @578AB5=B=8<8 4>

H;C=>2>3> A>:C, V <5A0;078= 7 =8E 282V;L=NTBLAO 70;56=> 2V4 @A5@54>28I0 7024O:8 ?>:@8BBN
C4@03VB>< L.

>;V=VG=V 40=V, I> 107CNBLAO =0 B@048FV9=8E 4>A;V465==OE I>4> 157?5:8, D0@<0:>;>3VW,
35=>B>:A8G=>ABV, :0=F5@>35==>ABV (=0 IC@0E) 01> B>:A8G=>ABV 4;O @5?@>4C:B82=>W A8AB5
<8, =5 2:07CNBL =0 >A>1;82C =5157?5:C 4;O ;N48=8.

C;> 2V4 =8@:>2C B>:A8G=VABL (=8@:>289 ?0?V;O@=89 =5:@>7 B0 ?>H:>465==O 5?VB5;VN 2 ?@>:A8
<0;L=8E :0=0;LFOE (Pars convoluta) 01> FV;>3> =5D@>=0) 2 4>A;V465==OE B>:A8G=>ABV ?@8
70AB>AC20==V ?>2B>@=8E 28A>:8E ?5@>@0;L=8E 4>7 <5A0;078=C. ;V=VG=0 206;82VABL F8E 40=8E
=52V4<<0.

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

030;L=V 2;0AB82>ABV <5c0;078=C

>3;8=0==O

>3;8=0==O <5A0;078=C T =0928I8< C ?@>:A8<0;L=V9 G0AB8=V :8H5G=8:C V =09=86G8< C
48AB0;L=V9 9>3> G0AB8=V.

V>B@0=AD>@<0FVO

5A0;078= <5B01>;V7CTBLAO O: 4>A8AB5<=> C A;87>2V9 >1>;>=FV :8H5G=8:C, B0: V 2 ?5GV=FV 4> D0@<0:>;>3VG=> =50:B82=>W N-0F5B8;-5-0A0;VF8;>2>W :8A;>B8 (N-AF-5-!). G5284=>, I> 0F5B8;N20==O =5 70;568BL 2V4 D5=>B8?C 0?0@0BC 0F5B8;N20==O E2>@>3>. 5O:5 0F5B8;N20==O B0:>6 2V41C20TBLAO 7024O:8 4VW 10:B5@V9 C B>2AB>

82545==O/5:A:@5FVO

5A0;078= V 9>3> <5B01>;VB N-AF-5-!282>4OBLAO 7 D5:0;VO<8 (>A=>2=0 G0AB8=0), =8@:0<8 (20@VNT 2V4 B8?C 70AB>AC20==O, D0@<0F52B8G=>W D>@<8 V H;OEC 282V;L=5==O <5A0;078=C, 2V4?>2V4=>) V 7 6>2GN (=57=0G=0 G0AB8=0). 8@:>20 5:A:@5FVO 2V41C20TBLAO ?5@5206=> C 283;O4V N-AF-5-!. ;87L:> 1 % 2V4 7030;L=>W 22545=>W >@0;L=> 4>78 <5A0;078=C 5:A:@5BCTBLAO C 3@C4=5 <>;>, 3>;>2=8< G8=>< C 283;O4V N-AF-5-!.

A>1;82>ABV B01;5B>: !0;>D0;L:C ?> 250 <3

>7?>4V;

><1V=>20=5 D0@<0:>AF8=B83@0DVG=>-D0@<0:>:V=5B8G=5 4>A;V465==O ?>:070;>, I> B01;5B:8 !0;>D0;L:C 250 <3 @>7G8=ONBLAO 2 ;;C1>2V9 :8HFV ?@81;87=> G5@57 3 - 4 3>48=8, O:I> WE ?@89=OB> @07>< 7 W65N. !5@54=V9 G0A 7=0E>465==O 2 H;C=:C AB0=>28BL ?@81;87=> 3 3>48=8. @81;87=> G5@57 7 3>48= B01;5B:8 4>AO30NBL >1>4>2>W :8H:8.

?>40;LH>A;V465==V =0 4>1@>2>;LFOE G0A 4C>45=>-V;50;L=>3> B@0=78BC AB0=>282 ?@81;87=> 3 3>48=8, B>4V O: <0:A8<0;L=0 :>=F5=B@0FVO 5-!2 ?@>A2VBV ;;C1>2>W :8H:8 2848= ?VA;O ?@89>: 7 W65N. @81;87=> 75 % 4>78 <5A0;078=C 4>AO30T B>2AB>3> :8H5G=8:C 2 =5<5B01>;V7>20=V9 D>@ >3;8=0==O

82V;L=5==O <5c0;078=C 7 B01;5B>: !0;>D0;L:C 250 <3 ?>G8=0TBLAO ?VA;O ;03-D078, I> B@820T 1;87L:> 3-4 3>48=. V: :>=F5=B@0FVW 2 ?;07AO30TBLAO ?@81;87=> G5@57 5 3>48= (V;5>F5:0;L=0 4V;O=:0) V AB0=>28BL ?@8 3 E 500<3 <5A0;078=C =0 4>1C (3 E 2 B01;5B:8 !0;>D0;L:C 250 <3) 70 AB0;8E C<>2 2,1 □ 1,7 □ 1,7

82545==O

@8 B@820;V9 B5@0?VW B01;5B:0<8 !0;>D0;L:C 250 <3 V7 70AB>AC20==O< 4>1>2>W 4>78 500 <3 <5A0;078=C B@8GV =0 45=L (70 AB0;8E C<>2) 7030;L=0 H284:VABL =8@:>2>3> 282545==O <5A0;078=C V N-F-5-!AB0=>28;0 ?@81;87=> 55 % (25;8G8=0 G5@57 24 3>48=8 ?VA;O >AB0==L>3> 22545==O). \$@0:FVO =5<5B01>;V7>20=>3> <5A0;078=C AB0=>28;0 1;87L:> 5 %. '0A =0?V2282545==O AB0=>282 0,7-2,4 3>48=8 (2 A5@54=L>□ 0,6 3>48=8) ?@8 4>7V <5A0;078=C 500 <3 B@8GV =0 45=L.

A>1;82>ABV B01;5B>: !0;>D0;L:C ?> 500 <3

>7?>4V;

><1V=>20=5 D0@<0:>AF8=B83@0DVG=>-D0@<0:>:V=5B8G=5 4>A;V465==O ?>:070;>, I> B01;5B:8 !0;>D0;L:C 500 <3 @>7G8=ONBLAO 2 ;;C1>2V9 :8HFV ?@81;87=> G5@57 3-4 3>48=8 B0 ?@81;87=> G5@57 4-5 3>48= - C =87EV4=V9 >1>4>2V9 :8HFV. 030;L=89 G0A ?@>E>465==O ?> B>2AB>28BL 1;87L:> 17 3>48=.

>3;8=0==O

82V;L=5==O <5c0;078=C 7 :8H:>2>@>7G8==8E B01;5B>: !0;>D0;L:C 500 <3 ?>G8=0TBLAO ?VA;O ;03-D078, I> B@820T 1;87L:> 3-4 3>48=. V: :>=F5=B@0FVW 2 ?;07AO30TBLAO ?@81;87=> G5@57 5 3>48= (V;5>F5:0;L=0 4V;O=:0) V AB0=>28BL ?@8 3 × 500<3 <5A0;078=C =0 4>1C (3 × 1 B01;5B:8 !0;>D0;L:C 500 <3) 70 AB0;8E C<>2 3,0 □ 1,6

3,4 □ 1,6

82545==O

@8 1030B>@07>2>AC20==V (3 × 1 B01;5BFV !0;>D0;L:C 500 <3 ?@>B03>< 2 4=V2; 1 :8H:>2>@>7G8==0 B01;5B:0 =0 B@5BV9 45=L = 45=L 4>A;V465==O) 7030;L=0 H284:VABL =8@:>2>3> 282545==O <5A0;078=C V N-F-5-!70 24 3>48=8 AB0=>28;0 ?@81;87=> 60 %. \$@0:FVO =5 <5B01>;V7>20=>3> <5A0;078=C ?VA;O >@0;L=>3> 22545==O AB0=>28;0 1;87L:> 10 %.

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

>:070==O.

□ 8@07:>289 :>;VB: ;V:C20==O 703>AB@5=L V ?@>DV;0:B8:0 @5F8482V2.

□ %2>@>10 @>=0: ;V:C20==O 703>AB@5=L.

@>B8?>:070==O.

V?5@GCB;82VABL 4><5A0;078=C, 4> 1C4L-O:>3> 7 :>=5=BV2 ?@5?0@0BC 01> 4> A0;VF8;0BV2, 28@07:>20 E2>@>10 H;C=:0 B0 420=04FOB8?0;>W :8H:8 2 AB04VW 703>AB@5==O, BO6:0 ?5GV=:>20 B0/01> =8@:>20 =54>AB0B=VABL, 35<>@03VG=89 4V0B57.

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

!75FV0;L=8E 4>A;V465=L ;V:0@AL:>W 270T<>4VW =5 ?@>2>48;>AL.
V4 G0A :>3> ;V:C20==O ?@5?0@0B<< !0;>D0;L: B0 070BV?@8=<<, 6-<5@:0?B?C@8=<< 01>
BV>3C0=V=<< C 450:8E 4>A;V465==OE 1C;> 2802;5=> 1V;LHC G0AB>BC AC?@5A82=8E 5D5:BV2, I>
=V18B> A2V4G8BL ?@> =0O2=VABL 270T<>4VW, >4=0: <5E0=V7< 270T<>4VW 2AB0=>2;5=89 =5
?>2=VABN. 5:>5=4CTBLAO @53C;O@=> :>=B@>;N20B8 @V25=L ;59:>F8BV2, 0 @568< 4>7C20==O
BV?>C@8=V2 A;V4 2V4:>@83C20B8.
40=V ?@> B5, I> <5A0;078= <>65 7=878B8 0=B8:>03C;OFV9=C 4VN 20@D0@8=C.
>6;825 ?>A8;5==O 3V?>3;V:5W 4VW ?>EV4=8E AC;LD>=V;A5G>28=8, B>:A8G=>W 4VW
<5B>B@5:A0BC. :B82=VABL DC@>A5=>;0:B>=C, AC;LD0=V;015=5F84C B0 AC;LDV=?V@07>=C) <>65
A;01H0B8. 5A0;078= <>65 ?>B5=FVN20B8 =51060=C 4VN 3;N:>:>@B8:>W4V2 =0 A;87>2C >1>;>=:C
H;C=:0, 7<5=HC20B8 2A<>:BC20==O 483>:A8=C.

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

5@54 ?>G0B:>< B0 ?V4 G0A ;V:C20==O =5>1EV4=> ?@>2>48B8 4>A;V465==O :@>2V (@>73>@=CB89
0=0;V7 :@>2V; ?0@0<5B@8 DC=:FVW ?5GV=:8, B0:V O: " 01> !"; :@50B8=V= C A8@>20BFV) V A5GV
(B5AB>2V AA04) =0 281V@ ;V:0@O. 5:>5=4CTBLAO ?@>2>48B8 :>=B@>;L G5@57 14 4=V2 2V4
?>G0B:C ;V:C20==O, ?>BV< 420-B@8 @078 7 V=B5@20;0<8 4 B86=V.
/I> @57C;LB0B8 4>A;V465=L =>@<0;L=V, @CB8==V ?5@52V@:8 4>AB0B=L> ?@>2>48B8 :>6=V 3
6 @>72820NBLAO V=HV 4>40B:>2V A8<8, 0=0;V78 =5>1EV4=> 7@>18B8 B5@2>.
>15@56=VABN A;V4 70AB>A>2C20B8 E2>@8< 7 ?>@CH5==O< DC=:FVW ?5GV=:8.
>B@V1=> 7 >15@56=VABN 70AB>A>2C20B8 !0;>D0;L: E2>@8< 7 ?>@CH5==O< DC=:FVW =8@>:.
5>1EV4=> @53C;O@=> :>=B@>;N20B8 DC=:FVN =8@>:, 0 A0<5 28BC A5G>28=8 :@>2V, :@50B8=V=C
C ?0FVT=BV2 7 ?@>B5W=C@VTN. @8 ?>3V@H5==V DC=:FVW =8@>: 2?@>4>26 ;V:C20==O A;V4
<0B8 =0 C207V V=4C:>20=C <5A0;078=<< B>:A8G=VABL 2V4=>A=> =8@>:.
%2>@V 7 ;535=528<8 70E2>@N20==O<8, 7>:@5<0 7 0AB<>N, ?>28==V 7=0E>48B8AL ?V4 =03;O4<<
;V:0@O ?@>BO3<< :C@AC ;V:C20==O B01;5B:0<8 !0;>D0;L:C.
%2>@V, O:V <0NBL @50:FVW 3V?5@GCB;82>ABV, 2;;NG0NG8 AC4<8, 3>AB@89 1V;L C 682>BV,
30@OG:C, A8;L=89 3>;>2=89 1V;L B0 28A8?0==O, =0 ?@5?0@0B8, I>
1 :8H:>2>@>7G8==0 B01;5B:0 !0;>D0;L:C
5<0T ?>B@518 7<5=HC20B8 4>7C20==O 4;O ?0FVT=BV2 ;VB=L>3> 2V:C.

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

0=8E I>4> 70AB>AC20==O :8H:>2>@>7G8==8E B01;5B>: !0;>D0;L:C 203VB=8<8 6V=:0<8
=54>AB0B=L>. @>B5 40=V ?@> 70AB>AC20==O <5A0;078=C 2 >1<565=V9 :V;L:>ABV 203VB=8E
2:07CNBL =0 2V4ACB=VABL =51060=8E 2?;82V2<5A0;078=C =0 ?5@51V3 203VB=>ABV 01> =0
74>@>2 O ?;>40 B0/01> =>2>=0@>465=>3>. 0 AL>3>4=V V=HV 5?V45;>3VG=V 40=V, I><0NBL
2V4=>H5==O 4> ?@5?0@0BC, =54>ABC?=V. >4=>3> 70AB>AC20==O C?@>4>26 203VB=>ABV
<5A0;078=C C 28A>:V9 4>7V (2-4 3 ?5@>@0;L=>) ?>2V4<<;O;>AO ?@> =8@:>2C =54>AB0B=VABL C
=>2>=0@>465=>3>. C;8 ?>2V4<<;5==O ?@> ?>@CH5==O 7 1>:C A8AB5<8 :@>2V (;59:>?5=VO, B@>
<1>F8B>?5=VO, 0=52>=0@>465=8E, <0B5@V O:8E 70AB>A>2C20;8 <5A0;078=
>A;V465==O =0 B20@8=0E ?@8 >@0;L=>
"01;5B:8 !0;>D0;L:C 500<3 =5>1EV4=> ?@89<0B8 ?@>BO3<< 203VB=>ABV ;8H5 B>4V, :>;8
?>B5=FV9=0 :>@8ABL 2V4 70AB>AC20==O ?5@52060B8<5 <>6;8289 @878:.
N-0F5B8;-5-0A0;VF8;>20 :8A;>B0 V, <5=H>N N, <5A0;078= 5:A:@5BCNBLAO C 3@C4=5 <>;>:. 0
AL>3>4=V T ;8H5 >1<565=89 4>A2V4 70AB>AC20==O ?@5?0@0BC 6V=:0< C ?5@V>4 3>4C20==O
3@C44N. 5 <>6=0 28;;NG8B8 @50:FV9 3V?5@GCB;82>ABV, B0:8E O: 4V0@50. B65, B01;5B:8
!0;>D0;L:C <>6=0 70AB>A>2C20B8 C ?5@V>4 3>4C20==O 3@C44N ;8H5 B>4V, :>;8 ?>B5=FV9=0
:>@8ABL 2V4 70AB>AC20==O ?5@52060B8<5 <>6;8289 @878:. /I> C 3@C4=>W 48B8=8 @>728=5BLAO
4V0@50, 3>4C20==O 3@C44N A;V4 ?@8?8=8B8.

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.
?:82 =0 740B=VABL :5@C20B8 02B>>1V;5< B0 ?@0FN20B8 7 V=H8<8 <5E0=V7<0<8 =5
A?>AB5@V302AO. # 28?04:0E, O:I> ?V4 G0A ;V:C20==O ?@5?0@0B× A?>AB5@V30TBLAO 70?0
<>@>G5==O, A;V4 CB@8<0B8AO 2V4 :5@C20==O B@0=A?>@B=8<8 70A>10<8 B0 @>1>B8 7 <5E0=V7
<0<8.

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

!0;>D0;L: 250 <3

>@>A;V B0 ?0FVT=B8 ;VB=L>3> 2V:C

;O B5@0?VW E@>=VG=8E 70?0;L=8E 70E2>@N20=L :8H5G=8:C (E2>@>10 @>=0, 28@07:>289 :>;VB)

<>6=0 70AB>A>2C20B8 O: B01;5B:8 !0;>D0;L: 250 <3, B0: V !0;>D0;L: 500 <3.

0;56=> 2V4 ;;V=VG=>W ?>B@518 2 :>6=>:@5<>@>A;8E @5:><5=4CNBLAO B0:V 4>1>2V 4>78:

	%2>@>10 @>=0, 703>AB@5==O	8@07:>289 :>;VB	
		03>AB@5==O	@>DV;0:B8:0 @5F8482V2/ B@820;0 B5@0?VO
5A0;078= (4VNG0 @5G>28=0)	1,5□4,5 3	1,5□3,0 3	1,5 3
!0;>D0;L;, B01;5B:8 ?> 250 <3	2V4 2 B01;5B>: × 3 @078 =0 4>1C 4> 6 B01;5B>: × 3 @078 =0 4>1C	2V4 2 B01;5B>: × 3 @078 =0 4>1C 4> 4 B01;5B>: × 3 @078 =0 4>1C	2 B01;5B:8 × 3 @078 =0 4>1C

VB8 2V:>× 4> 6 @>:V2

"01;5B:8 !0;>D0;L:C 250 <3 =5 <>6=0 70AB>A>2C20B8 4VBO< 2V:>× 4> 6 @>:V2, >A;V;L:8 4>A2V4
70AB>AC20==O ?@5?0@0BC C FV9 2V:>2V9 3@C?V =54>AB0B=V9.

VB8 2V:>× 2V4 6 @>:V2

@8 3>AB@8E =0?040E, 70;56=> 2V4 BO6:>ABV 70E2>@N20==O, ?@87=0G0NBL 30-50 <3 <5A0;078=C
/:3 <0A8 BV;0/4>1C, @>7?>4V;82H8 =0 3 ?@89×8. 0:A8<0;L=0 4>70: 75 <3 <5A0;078=C/:3 <0A8 BV;0
/4>1C. 030;L=0 4>1>20 4>70 =5 ?>28==0 ?5@528IC20B8 <0:A8<0;L=C 4>7C 4;O 4>@>A;8E.

;O ?@>DV;0:B8:8 @5F8482V2 (=5A?5F8DVG=89 28@07:>289 :>;VB) ?@5?0@0B ?@87=0G0TBLAO
V=482V4C0;L=>, ?>G8=0NG8 7 15-30 <3 <5A0;078=C/:3 <0A8 BV;0/4>1C, @>7?>4V;5=8E =0 2-3 ?@89>
<8. 030;L=0 4>1>20 4>70 =5 ?>28==0 ?5@528IC20B8 <0:A8<0;L=C 4>7C 4;O 4>@>A;8E.

7030;V 4VBO< 7 <0A>N BV;0 4> 40 :3 @5:><5=4CTBLAO ?@89<0B8 ?>:>28=C 4>78 4;O 4>@>A;8E,
4VBO< 7 <0A>N BV;0 ?>=04 40 :3 728G09=C 4>7C 4;O 4>@>A;8E.

;O ;V:C20==O 4VB59 2V:>× 2V4 6 @>:V2 @5:><5=4CNBLAO B0:V 4>1>2V 4>78:

	%2>@>10 @>=0, 703>AB@5==O	8@07:>289 :>;VB	
		03>AB@5==O	@>DV;0:B8:0 @5F8482V2/ B@820;0 B5@0?VO
5A0;078= (4VNG0 @5G>28=0)	0,75□2,25 3	0,75□1,5 3	0,75 3
!0;>D0;L;, B01;5B:8 ?> 250 <3	2V4 1 B01;5B:8 × 3 @078 =0 4>1C 4> 3 B01;5B>: × 3 @078 =0 4>1C	2V4 1 B01;5B:8 × 3 @078 =0 4>1C 4> 2 B01;5B>: × 3 @078 =0 4>1C	?> 1 B01;5BFV × 3 @078 =0 4>1C

!0;>D0;L: 500 <3

/:I> @5:><5=4>20=0 4>70 ?5@528ICT 1,5 3 <5A0;078=C =0 4>1C, 70728G09 70AB>A>2CNBL B01;5B:8 !0;>D0;L:C 500 <3.

>@>A;V B0 ?0FVT=B8 ;VB=L>3> 2V:C

0;56=> 2V4 ;;V=VG=>W ?>B@518 2 :>6=>:@5<><5=4CNBLAO B0:V 4>1>2V 4>78:

	%2>@>10 @>=0, 703>AB@5==O	8@07:>289 :>;VB	
		03>AB@5==O	@>DV;0:B8:0 @5F8482V2/ B@820;0 B5@0?VO
5A0;078= (4VNG0 @5G>28=0)	1,5□4,5 3	1,5□3,0 3	1,5 3
!0;>D0;L;, B01;5B:8 ?> 500 <3	2V4 1 B01;5B:8 × 3 @078 =0 4>1C 4> 3 B01;5B>: × 3 @078 =0 4>1C	2V4 1 B01;5B:8 × 3 @078 =0 4>1C 4> 2 B01;5B>: × 3 @078 =0 4>1C	?> 1 B01;5BFV 3 @078 =0 4>1C

VB8 2V:>< 4> 6 @>:V2

"01;5B:8 !0;>D0;L:C 500 <3 =5 <>6=0 70AB>A>2C20B8 4VBO< 2V:>< 4> 6 @>:V2 G5@57 2V4ACB=VABL 4>A2V4C 70AB>AC20==O ?@5?0@0BC C FV9 2V:>2V9 3@C?V.

VB8 2V:>< 2V4 6 @>:V2

@8 3>AB@8E =0?040E, 70;56=> 2V4 BO6:>ABV 70E2>@N20==O, ?@87=0G0NBL 30-50 <3 <5A0;078=C /:3 <0A8 BV;0/4>1C, @>7?>4V;82H8 =0 3 ?@89<8. 0:A8<0;L=0 4>70: 75 <3 <5A0;078=C/:3 <0A8 BV;0 /4>1C. 030;L=0 4>1>20 4>70 =5 ?>28==0 ?5@528IC20B8 <0:A8<0;L=C 4>7C 4;O 4>@>A;8E. ;O ?@>DV;0:B8:8 @5F8482V2 (=5A?5F8DVG=89 28@07:>289 :>;VB) ?@5?0@0B ?@87=0G0TBLAO V=482V4C0;L=>, ?>G8=0NG8 7 15-30 <3 <5A0;078=C/:3 <0A8 BV;0/4>1C, @>7?>4V;5=8E =0 2-3 ?@89> <8. 030;L=0 4>1>20 4>70 =5 ?>28==0 ?5@528IC20B8 <0:A8<0;L=C 4>7C 4;O 4>@>A;8E. 7030;V 4VBO< 7 <0A>N BV;0 4> 40 :3 @5:><5=4CTBLAO ?@89<0B8 ?>;>28=C 4>78 4;O 4>@>A;8E, 4VBO< 7 <0A>N BV;0 ?>=04 40 :3 728G09=C 4>7C 4;O 4>@>A;8E. 0;56=> 2V4 ;;V=VG=8E ?>B@51 V <0A8 BV;0 (4> 40 :3) 48B8=8 A;V4 ?@89=OB8 @VH5==O, O:89 284 B01;5B>: A;V4 70AB>A>2C20B8 !0;>D0;L: 250 <3 01> !0;>D0;L: 500 <3.

030;L=V @5:><5=40FVW I>4> 70AB>AC20==O

"01;5B:8 !0;>D0;L:C ?>B@V1=> ?@89<0B8 2@0=FV, 2 >1V4 V 225G5@V 70 1 3>48=C 4> W48. "01;5B:8 ?>B@V1=> :>2B0B8 FV;8<8, =5 @>76>2CNG8, 7 4>AB0B=L>N :V;L:VABN @V48=8.

/: ?@8 3>AB@8E AB0=0E ?@8 70?0;5==V, B0: V ?@8 B@820;>AC20==V 4;O 4>AO3=5==O 1060=>3> B5@0?52B8G=>3> 5D5:BC B01;5B:8 !0;>D0;L:C ?>B@V1=> ?@89<0B8 @53C;O@=> V ?>ABV9=>.

"@820;VABL 70AB>AC20==O 287=0G0T ;V:0@.

0728G09 703>AB@5==O ?@8 28@07:>2>;V BV V E2>@>1V @>=0 AB8E0T G5@57 8-12 B86=V2.

;O ?@>DV;0:B8:8 @5F8482V2 28@07:>2>3> :>;VBC 4>7C <>6=0 7=878B8 4> 1,5 3 <5A0;078=C =0 4>1C (4>@>A;V V 4VB8 7 <0A>N BV;0 ?>=04 40 :3) 4> 0,75 <3 <5A0;078=C =0 4>1C (4VB8).

@8

@V4:VA=8E 28?04:0E C E2>@8E, I> ?V4;O30;8 @575:FVW :8H5G=8:C/EV@C@3VG=>2>->1>4>2V9 4V;O=FV 7 2840;5==O< ;;C1>2>->1>4>2>3> ;;0?0=0, A?>AB5@V30;8, I> B01;5B:8 !0;>D0;L:C 282>48;8AL =5@>7G8=5=8<8 7 :0;>< 2=0A;V4>: =04B> H284:>3> ?@>E>465==O G5@57 :8H5G=8:.

VB8.

"01;5B:8 !0;>D0;L:C =5 <>6=0 70AB>A>2C20B8 4VBO< 2V:>< 4> 6 @>:V2, B> 4>A2V4 70AB>AC20==O ?@5?0@0BC C FV9 2V:>2V9 3@C?V =54>AB0B=V9.

5@54>7C20==O.

>B5?5@ ?@> 28?04:8 V=B>:A8:0FVW B0 A?5F8DVG=V 0=B84>B8 =5 ?>2V4<;O;>AL.

40=V ?@> 28?04:8 ?5@54>7C20==O (=0?@8;:04 =02<8A=5 A0<>3C1AB2> 28A>:>N ?5@>@0;L=>N 4>7>N <5A0;078=C), O:V =5 2:07CNBL =0 =8@:>2C 01> ?5GV=:>2C B>:A8G=VABL. !?5F8DVG=>3> 0=B84>BC =5 VA=CT, ;V:C20==O ?>28==> 1CB8 A8<0B8G=8< B0 ?V4B@81EV4=>ABV 70AB>A>2CNBL 2=CB@VH=L>25==C V=DC7VN 5;5:B@>;VBV2 (?@8289 4VC@57).

>1VG=V @50:FVW.

!8AB5<0 >@30=V2	'0AB>B0 2V4?>2V4=> 4> MedDRA	
	@V4:VA=V (□ 1/10000; □ 1/1000)	4C65 @V4:VA=V (□ 1/10000)
!8AB5<0 :@>2V V ;V		2V (0?;0AB8G=0 0=5F8B>7, ?0=F8B>?5=VO, =59B@>?5=VO, ;59:>?5=VO, B@> <1>F8B>?5=VO)
5@2>20 A8AB5<0	>;>2=89 1V;L, 70?0 <>@>G5==O	5@8D5@8G=0 =59@>?0BVO, 4>1@>O:VA=0 2=CB@VH=L>G5@5?=0 3V?5@B5=7VO (C 4VB59 C ?C15@B0B=>4V)
!5@F52>-AC48==0 A8AB5<0	V>:0@48B, ?5@8:0@48B	
@30=8 48E0==O, 3@C4=>W ;VB:8 B0 A5@54>ABV==O		;5@3VG=V B0 DV1@>7=V @50:FVW ;535=V2 (2;;NG0NG8 48A?=>5, :0H5;L, 1@>=E>A?07<, 0;L25>;VB, ;535=52C 5>7>=>DV;VN, V=DV;LB@0FVN ;535=V2, ?=52<>=VB, ?;52@8B)
(;C=:>2>-:8H:>289 B@0:B	14>	>AB@89 ?0=:@50B8B
8@:8		>@CH5==O DC=:FVW =8@>;, 2;;NG0NG8 3>AB@89 V E@>=VG=89 V=B5AB8=0;L=89 =5D@8B, =5D@>B8G=89 A8=4@< V =8@:>2C =54>AB0B=VABL
(:V@0 V WW ?>EV4=V		;>?5FVO
!5;5B=>-<O7>20 A8AB5<0 B0 A?>;CG=V B:0=8=8		V0;3VO, 0@B@0;3VO, AC4><8
		50:FVW 3V?5@GCB;82>ABV, 2;;NG0NG8 0;5@3VG=V 28A8?0==O, <548:0 <5=B>7=C 30@OG:C, 2>2G0:>?>4V1=89 A8=4@> <, ?0=:>;VB, =01@O: 2V=:5
5GV=:0 V 6>2G=89		
5?@>4C:B82=0 A8AB5<0		;V3>A?5@1>@>B=0)

"0:>6 <>6;82V: 2B<0, ?0@5AB57VW, <5B35<>3;>1V=5A8;5==O A8;VBC.
5E0=V7< @>728B:C :0@48BC, ?5@8:0@48BC, ?0=:@50B8BC, =5D@8BC V 35?0B8BC C 72O7:C V7
70AB>AC20==O< <5A0;078=C =52V4><89; 2V= <65 <0B8 0;5@3VG=C 5BV>;>3VN.
!;V4 707=0G8B8, I> 45O:V 7 F8E @>7;04V2 <>6=0 ?>OA=8B8 A0<8< 70?0;5==O< :8H5G=8:C.

"5@ABV.3 @>:8.

5 <>6=0 70AB>A>2C20B8 ?VA;O 70:V=G5==O B5@ABV, 707=0G5=>3> =0 C?0:>2FV.

#<>28 715@V30==O. 15@V30B8 C =54>ABC?=>° !.

#?0:>2:0. > 10 B01;5B>: C 1;VAB5@V; ?> 5 01> 10 1;VAB5@V2 C :>@>1FV 7 :0@B>=C.

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

8@>1=8:.

@. \$0;L: \$0@<0 <1%.

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

O9=5=2515@HB@0AA5 5, -79108 \$@091C@3, V<5GG8=0.