

!" #&/
4;O <548G=>3> 70AB>AC20==O ?@5?0@0BC
-!" \$
(!ARBAMAZEPIN-ASTRAPHARM)

!;:04:
4VNG0 @5G>28=0: carbamazepine;
1 B01;5B:0 :0@10<075?V=C 200 <3;
4>?>28=8: F5;N;>70 :@8AB0;VG=0, ?>2V4=>, <03=VN AB50@0B, =0B@VN :@>A:0@<5;>70.

V:0@AL:0 D>@<0. "01;5B:8.

\$0@<0:>B5@0?52B8G=0 3@C?0.
@>B85?V;5?B8G=V 70A>18. >4 "N03A F01.

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

>:070==O.

□ □?V;5?AVO:

A:;04=V 01> ?@>ABV ?0@FV0;L=V AC4<=V =0?048 (V7 2B@0B>N 01> 157 2B@0B8 A2V4<>ABV)

V7 2B>@8==>N 35=5@0;V70FVTN 01> 157 =5W;

35=5@0;V7>20=V B>=V:>.;>=VG=V AC4<=V =0?048;

7@<8 AC4<=8E =0?04V2.

0@10<075?V=-□AB@0D0@< <>6=0 70AB>A>2C20B8 O: <=>B5@0?VN, 0 B0:>6 C A:;04V :>

<1V=>20=>W B5@0?VW.

□ >AB@V <0=V0:0;L=V AB0=8; ?V4B@8;O@=8E 0D5:B82=8E @>7;040E 7 <5B>N ?@>DV;0:B8:8
703>AB@5=L 01> 4;O >A;01;5==O ;V=VG=8E ?@>O2V2 703>AB@5==O.

□ !8=4@<> 0;:>3>;L=>W 01AB8=5=FWW.

□ 4V>?0B8G=0 =52@0;3VO B@V9G0AB>3> =5@20 V =52@0;3VO B@V9G0AB>3> =5@20 ?@8
@>7AVO=>7V (B8?>20 B0 0B8?>20).

□ 4V>?0B8G=0 =52@0;3VO O78:>3;>B:>2>3> =5@20.

@>B8?>:070==O.

V428I5=0 GCB;82VABL 4> :0@10<075?V=C, 4> ?>4V1=8E C EVH5==V ;V:0@AL:8E 70A>1V2 (B0:8E O:

B@8F8;;VG=V 0=B845?@5A0=B8) 01> 4> 1C4L-O:>3> V=H>3> :=5=B0 ?@5?0@0BC;

0B@V>25=B@8:C;O@=0 1;>:040;

?@83=VG5==O :VAB:>2>3><>7:C 2 0=0<=57V;

?5GV=:>20 ?>@DV@VO (=0?@8::04 3>AB@0 V=B5@@@DV@VO, 7@DV@VO, ?V7=O ?>@DV@VO

H:V@8) 2 0=0<=57V;

>4=>G0A=5 70AB>AC20==O 7 V=3V1VB>@0<8 <=>0:A84078 (MAO).

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

0@10<075?V=-□AB@0D0@< ?@87=0G0NBL ?5@>@0;L=>; 70728G09 4>1>2C 4>7C ?@5?0@0BC

@>7?>4V;ONBL =0 2 01> 3 ?@89<8. @5?0@0B <>6=0 ?@89<0B8 ?V4 G0A, ?VA;O W48 01> C ?@<0<8

W6V, 70?820NG8 =525;8:>N ;V:L.VABN @V48=8, =0?@8::04 A:;O=:>N 2>48.

5@54 ?>G0B:<< ;V:C20==O ?0FVT=B8, O:V 70 ?>E>465==O< ?>B5=FW9=> T =>AVO<8 0;5;O HLA-

*3101 ?> <>6;82>ABV ?>28==V ?@>9B8 >1AB565==O =0 =0O2=VABL 0;5;O, >A:V;L:8 C FL>

?V;5?AVO

V:C20==O @>7?>G8=0NBL V7 70AB>AC20==O =87L:>W 4>1>2>W 4>78, ?>ABC?>2> ?V428ICNG8 V
 :>@83CNG8 4>7C 7 C@0EC20==O< ?>B@51 :>6=>3> ?0FVT=B0.
 ;O ?V41>@C >?B8<0;L=>W 4>78 ?@5?0@0BC 287=0G0NBL @V25=L :0@10<075?V=C C ?;072V.
 A>1;82> C 28?04:C :><1V=>20=>W B5@0?VW B5@0?52B8G=V 4>78 A;V4 @>7@0EC20B8 =0 >A=>2V
 @V2=O :0@10<075?V=C C ?;072V B0 5D5:B82=>ABV.
 >@>A;V: @5:><5=4>20=0 ?>G0B:>20 4>70 ?@5?0@0BC AB0=>28BL ?> 100-200 <3 1-2 @078 =0 4>1C.
 >BV< 4>7C ?>2V;L=> ?V428ICNBL 4> 4>AO3=5==O >?B8<0;L=>3> 5D5:BC; G0AB> 4>1>20 4>70
 AB0=>28BL 800-1200 <3. 5O:8< ?0FVT=B0< <>65 1CB8 ?>B@V1=0 4>70 :0@10<075?V=C 1600 <3 01>
 =02VBL 2000 <3 =0 4>1C.
 0FVT=B8 ;VB=L>3> 2V:C: ?0FVT=B0< ;VB=L>3> 2V:C G5@57 <>6;82C ;V:0@AL:C 270T<>4VN 4>7C
 ?@5?0@0BC A;V4 ?V418@0B8 72065=>.
 VB8: ;V:C20==O <>6=0 @>7?>G8=0B8 V7 70AB>AC20==O 100 <3/4>1C; 4>7C ?V428ICNBL ?>ABC?>2>
 :>6=>3> B86=O =0 100 <3.
 28G09=0 4>70 ?@5?0@0BC AB0=>28BL 10-20 <3/:3 <0A8 BV;0 =0 4>1C (70 :V;L:0 ?@89>

V: 48B8=8	>1>20 4>70
5-10 @>:V2	400-600 <3 (70 2-3 ?@89><8)
10-15 @>:V2	600-1000 <3 (70 2-5 ?@89>

;O 4VB59 2V:>< 2V4 15 @>:V2 ?@87=0G0NBL 4>78 O: 4;O 4>@>A;8E.
 /:I> <>6;82>, 0@10<075?V=-□AB@0D0@< A;V4 ?@87=0G0B8 O: <>=>B5@0?VN, 0 C @07V
 70AB>AC20==O 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 @5:><5=4CTBLAO @568< B0:>3> 6 A0<>3>
 ?>ABC?>2>3> ?V428I5==O 4>78 ?@5?0@0BC.
 @8 ?@87=0G5==V :0@10<075?V=C 4>40B:>2> 4> ?>B>G=>W ?@>B85?V;5?B8G=>W B5@0?VW 4>7C
 ?@5?0@0BC A;V4 ?>ABC?>2> ?V428IC20B8, =5 778 70AB>A>20=8E ?@>B85?V;5?B8G=8E
 ?@5?0@0BV2 01>, C @07V =5>1EV4=>ABV, :>@83CNG8 WW.
 >AB@V <0=V0:0;L=V AB0=8 B0 ?V4B@8;O@=8E 0D5:B82=8E @>7;040E
 V0?07>= 4>7 ?@81;87=> 2V4 400 4> 1600 <3 =0 4>1C; 70728G09 2V4 400 4> 600 <3 =0 4>1C,
 @>7?>4V;5=8E =0 2-3 ?@89><8. @8 3>AB@><5=4CTBLAO 4>AB0B=L> H284:5 ?V428I5==O 4>78,
 B>4V O: 7 <5B>N 70157?5G5==O >?B8<0;L=>W B>;5@0=B=>ABV C @0W B5@0?VW ?@8 1V?>;O@=8E
 @>7;040E @5:><5=4>20=5 ?>ABC?>25 ?V428I5==O <0;8<8 4>70<8.
 !8=4@>< 0;:>3>;L=>W 01AB8=5=FVW
 !5@54=O 4>70 ?> 200 <3 3 @078 =0 4>1C. # BO6:8E 28?04:0E ?@>BO3>< ?5@H8E :V;L:>E 4=V2 4>7C
 <>6=0 ?V428I8B8 (=0?@8;:04 4> 4>78 ?> 400 <3 3 @078 =0 4>1C). @8 BO6:8E ?@>O20E 0;:>3>;L=>W
 01AB8=5=FVW ;V:C20==O @>7?>G8=0NBL :><1V=0FVTN :0@10<075?V=C V7 A540B82=>-A=>4V9=8
 <8 ?@5?0@0B0<8 (=0?@8;:04 V7 ;>5BV07>;><, E;>@4V075?>:A84><), 4>B@8: I>4> 4>7C20==O. VA;O
 7025@H5==O 3>AB@>W D078 ?@5?0@0B 0@10<075?V=-□AB@0D0@< <>6=0 70AB>A>2C20B8 O:
 <>=>B5@0?VN.
 4V>?0B8G=0 =52@0;3VO B@V9G0AB>3> =5@20 V =52@0;3VO B@V9G0AB>3> =5@20 ?@8
 @>7AVO=>7V (B8?>20 B0 0B8?>20). 4V>?0B8G=0 =52@0;3VO O78:>3>;>B:>2>3> =5@20
 >G0B:>20 4>70 ?@5?0@0BC 0@10<075?V=-□AB@0D0@< AB0=>28BL 200-400 <3 =0 4>1C (100 <3 2
 @078 =0 4>1C 4;O ?0FVT=V2 ;VB=L>3> 2V:C). W ?>2V;L=> ?V428ICNBL 4> 7=8:=5==O 1>;L>28E
 2V4GCBBV2 (70728G09 4> 4>78 ?> 200 <3 3-4 @078 =0 4>1C). ;O 1V;LH>ABV ?0FVT=V2 4>70
 ?@5?0@0BC 200 <3 3 01> 4 @078 =0 4>1C T 4>AB0B=L>N 4;O ?V4B@8;VA=>3> AB0=C. # 45O:8E
 28?04:0E <>65 1CB8 =5>1EV4=>N 4>1>20 4>70 ?@5?0@0BC 0@10<075?V=-□AB@0D0@< 1600 <3. VA;O
 7=8:=5==O 1>;L>28E 2V4GCBBV2 4>7C ?>ABC?>2> 7=86CNBL 4> W.

>1VG=V @50:FVW.

0 ?>G0B:C ;V:C20==O :0@10<075?V=>< 01> ?@8 70AB>AC20==V =04B> 25;8:>W ?>G0B:>2>W 4>78
 ?@5?0@0BC, 0 B0:>6 ?@8 ;V:C20==V ?0FVT=V2 ;VB=L>3> 2V:C 4C65 G0AB> 28=8:0NBL =51060=V
 @50:FVW 7 1>:C F5=B@0;L=>W =5@2>2>W A8AB5<8 (&!) (70?0<>@>G5==O, 3>;>2=89 1V;L, 0B0:AVO,
 A>;82VABL, 7030;L=0 A;01:VABL, 48?;>?VO), 7 1>:C B@02=>3> B@0:BC (=C4>B0, 1;N20==O) 01>
 0;5@3VG=V H:V@=V @50:FVW.
 >7>70;56=V =51060=V @50:FVW 70728G09 <8=0NBL ?@>BO3>< :V;L:>E 4=V2 O: A?>=B0==>, B0: V
 ?VA;O B82>3> 7=865==O 4>78 ?@5?0@0BC. >728B>: =51060=8E @50:FV9 7 1>:C &! <>65 1CB8

=0A;V4:>< 2V4=>A=>3> ?5@54>7C20==O ?@5?0@0BC 01> 7=0G=8E :>;820=L :>=F5=B@0FVW :@010
<075?V=C C ?;072V. # B0:8E 28?04:0E @5:><5=4CTBLAO ?@>2>48B8 <=>VB>@8=3 @V2=O :0@10
<075?V=C C ?;072V B0 @>7?>4V;8B8 4>1>2C 4>7C ?@5?0@0BC =0 1V;LH 4@V1=V (=0?@8::04 =0 3-4)
>:@578.

I>:C A8AB5<8 :@>2V: ;59:>?5=VO, B@><1>F8B>?5=VO, 5>78=>DV;VO, ;59:>F8B>7, ;V045=>?0BVO,
45DVF8B D>;VT2>W :8A;>B8, 03@0=C;>F8B>7, 0?;0AB8G=0 0=5?5=VO, 5@8B@>F8B0@=0 0?;07VO,
0=5AB@0 V=B5@@DV@VO, 7@DV@VO, ?V7=O ?>@DV@VO H:V@8, @5B8:C;>F8B>7, 35<>;VB8G=0
0=5

I>:C VW A8AB5<8: @30==0 3V?5@GCB;82VABL C?>2V;L=5=>3> B8?C 7 30@OG:>N, H:V@=8<8
28A8?0==O<8, 20A:C;VB><, ;V?0BVTN; >7=0:0<8, I> =0304CNBL ;V:0@40, B>2AB>W :8H:8);
0A5?B8G=89 <5=V=3VB 7 ;;>=CA>< V ?5@8D5@8G=>N 5>78=>DV;VTN; 0=0DV;0:B8G=0 @50:FVO,
0=3V>=52@>B8G=89 =01@O:, 3V?>30<<03;>1C;V=5

I>:C 5=4>:@8==>W A8AB5<8: =01@O:8, 70B@8A<>;O@=>ABV ?;07<8 2=0A;V4>: 5D5:BC, ?>4V1=>3>
4> 4VW 0=B84VC@5B8G=>3> 3>@<>=C, I> C ?>>48=>:8E 28?04:0E ?@872>48BL 4>
3V?5@3V4@0B0FVW, O:0 AC?@>2>46CTBLAO ;5B0@3VTN, 1;N20==O<, 3>;>2=8< 1>;5<,
A?;CB0=VABN A2V4><>ABV V =52@>;>3VG=8<8 @>7;040<8; ?V428I5==O @V2=O ?@>;0:B8=C :@>2V,
O:5 <>65 AC?@>2>46C20B8AL 01> =5 AC?@>2>46C20B8AO B0:8<8 ?@>O20<8, O: 30;0:B>@50, 3V=5:>
<0ABVO, ?>@CH5==O <5B01>;V72>W B:0=8=8 (7=865==O @V2=O :0;LFVN V 25-
3V4@>:A8E>;5:0;LF8D5@>;C C ?;072V), I> ?@872>48BL 4> >AB5><0;OFVW/>AB5>?>@>7C;
?V428I5==O :>=F5=B@0FVW E>;5AB5@8=C, 2;;NG0NG8 E>;5AB5@8= ;V?>?@>B5W4V2 28A>:>W
IV;L=>ABV V B@83;VF5@848.

I>:C >128=: =54>AB0B=VABL D>;0BV2, 7=865==O 0?5B8BC, 3>AB@0 ?>@DV@VO (3>AB@0 V=B5@
@DV@VO B0 7@DV@VO), =53>AB@0 ?>@DV@VO (?V7=O ?>@DV@VO H:V@8).

I>:C ?A8EV:8: 30;NF8=0FVW (7>@>2V 01> A;CE>2V), 45?@5AVO, 2B@0B0 0?5B8BC, =5A?>:V9,
03@5A82=VABL, 068B0FVO, A?;CB0=VABL A2V4><>ABV, 0:B820FVO ?A8E>7C.

I>:C =5@2>2>W A8AB5<8: 70?0<>@>G5==O, 0B0:AVO, A>=:82VABL, 7030;L=0 A;01:VABL, 3>;>2=89
1V;L, 48?;>?VO, 0=><0;L=V <8<>2V;L=V @CE8 (=0?@8::04 B@5<>@, «B@V?>B;8289» B@5<>@,
48AB>=VO, B8:), =VAB03<, >@>D0FV0;L=0 48A:V=57VO, ?>@CH5==O @CEC >G59, ?>@CH5==O
<>2;5==O (=0?@8::04 4870@B@VO 01> =5@>71V@;820 <>20), E>@5>0B5B>7, ?5@8D5@8G=0
=52@>?0BVO, ?0@5AB57VW, <07>20 A;01:VABL, ?0@57, ?>@CH5==O A<0:>28E 2V4GCBBV2,
7;>O:VA=89 =59@>;5?B8G=89 A8=4@<, 0A5?B8G=89 <5=V=3VB 7 ;;>=VTN B0 ?5@8D5@8G=>N
5>78=>DV;VTN, 48A3527VO.

I>:C >@30=V2 7>@C: ?>@CH5==O 0:><>40FVW (=0?@8::04 70BC<0=5==O 7>@C), ?>=N=:B82VB,
?V428I5==O 2=CB@VH=L>>G=>3> B8A:C.

I>:C >@30=V2 A;CEC: @>7;048 A;CEC, =0?@8::04 472V= C 2CE0E, ?V428I5==O A;CE>2>W
GCB;82>ABV, 7=865==O A;CE>2>W GCB;82>ABV, ?>@CH5==O A?@89=OBBO 28A>B8 72C:C.

I>:C A5@F52>-AC48==>W A8AB5<8: ?>@CH5==O 2=CB@VH=L>A5@F52>W ?@>2V4=>ABV;
0@B5@V0;L=0 3V?5@B5=7VO 01> 0@B5@V0;L=0 3V?>B5=7VO, 1@048:0@4VO, 0@8B
25=B@8:C;O@=0 1;>:040 V7 A8=:>?5, F8@:C;OB>@=89 :>;0?A, 70ABV9=0 A5@F520 =54>AB0B=VABL,
703>AB@5==O VH5W E2>@>18, B@><1>D;51VB, B@><1>5<1>;VO (=0?@8::04 5<1>;VO AC48=
;535=L).

I>:C 48E0;L=>W A8AB5<8: @50:FVW 3V?5@GCB;82>ABV 7 1>:C ;535=V2, I> E0@0:B5@87CNBLAO
30@OG:>N, 7048H:>N, ?=52<>=VB>< 01> ?=52<>=VTN.

I>:C B@02=>3> B@0:BC: =C4>B0, 1;N20==O, ACEVABL C @>BV, 4V0@50, 70?>@, 014A8B, AB>
<0B8B, ?0=:@50B8B.

I>:C 35?0B>1V;V0@=>W A8AB5<8: ?V428I5==O @V2=O 30<<0-3;CB0: V=4C:FVW D5@<5=BC
?5GV=:8), I> 70728G09 =5 <0T ;;V=VG=>3> 7=0G5==O; ?V428I5==O @V2=O ;C6=>W D>AD0B078
:@>2V; ?V428I5==O @V2=O B@0=A0;5AB0B8G=>3>, ?0@5=EV<0B>7=>3> (35?0B>F5;N;O@=>3>) 01> 7
3> B8?V2; A8=4@< 7=8=:5==O 6>2G=8E H;OEV2; 6>2BO=8FO; 3@0=C;5<0B>7=89 35?0B8B;
?5GV=:>20 =54>AB0B=VABL.

I>:C H:V@8: 0;5@3VG=89 45@<0B8B, :@>?820=:0, V=>4V C BO6:V9 D>@;V0B82=89 45@<0B8B;
5@8B@>45@@<=0 B0 2C7;8:>20 5@8B5<0; ?>@CH5==O ?V3<5=B0FVW H:V@8; ?C@?C@0; 0=:5;
?V428I5=0 ?VB;82VABL; ?>A8;5=5 28?040==O 2>;>AAO; 3V@ACB87

I>:C :VAB:>2>-<O7>2>W A8AB5<8: <O7>20 A;01:VABL, 0@B@0;3VW,<O7>289 1V;L, A?07<8 <O7V2, ?>@CH5==O :VAB:>2>3><5B01>;V7:A8E>;5;0;LF8D5@>;C C ?;072V, I> <>65 ?@8725AB8 4> >AB5> <0;OFVW 01> >AB5?>@>7C).

I>:C A5G>284V;L=>W A8AB5<8: BC1C;>V=B5@AB8FV0;L=89 =5D@8B, =8@:>20 =54>AB0B=VABL, ?>@CH5==O DC=:FVW =8@>:(=0?@8::04 0;L1C28?CA:0==O, 70B@8

I>:C @5?@>4C:B82=>W A8AB5<8: AB0B520 48ADC=:FVO/VB5=FVO/5@5:B8;L=0 48ADC=:FVO, ?>@CH5==O A?5@<0B>35=57C (7V 7=865==O< :V;L:>ABV/@CE;82>ABV A?5@<0B>7>W4V2).

030;L=V ?>@CH5==O: 7030;L=0 A;01:VABL.

01>@0B>@=V ?>:07=8:8: ?V428I5==O @V2=O 30<<0-3;NB028E D5@<5=BV2), O:5 70728G09 =5 <0T ;V=VG=>W 7=0G8<>ABV; 71V;LH5==O @V2=O ;C6=>W D>AD0B078 2 :@>2V; 71V;LH5==O @V2=O B@0=A0>G=>3> B8A:C; 71V;LH5==O @V2=O E>;5AB5@8=C C :@>2V; 71V;LH5==O @V2=V2 ;V?>@>B5W=V2 28A>:>W IV;L=>ABV; 71V;LH5==O @V2=V2 B@83;VF5@84V2 C :@>2V; 707=8:V2 DC=:FVW I8B>284=>W 70;>78: 7=865==O @V2=O L-B8@>:A8=C (FT4, T4, T3) V ?V428I5==O @V2=O B8@5>AB83> 3>@<>=C, I>, O: ?@028;>, =5 AC?@>2>46CTBLAO ;V=VG=8<8 ?@>O20<8; 71V;LH5==O @V2=O ?@>;0:B8=C 2 :@>2V, 3V?>30<<03;>1C;V=5

>1VG=V @50:FVW, 28O2;5=V C ?>AB@5TAB@0FV9=89 ?5@V>4.

=D>@<0FVO ?@> =86G5707=0G5=V ?>1VG=V @50:FVW 1C;0 >B@8<0=0 ?@8 ?>AB@5TAB@0FV9=> AC20==V ?@5?0@0BC 7V A?>=B0==8E ?>2V4<;5=L B0 A?5FV0;L=>W ;VB5@0BC@8. A:V;L:8 ?>2V4< <;5==O A?>=B0==V, =5<>6;82> 2AB0=>28B8 B>G=C :V;L:VABL ?0FVT=V2 B0 4>AB>2V@=> >FV=8B8 G0AB>BC 28=8:=5==O ?>1VG=8E @50:FV9.

=D5:FVW B0 V=207VW: @50:B820FVO 2V@CAC 35@?5AC ;N48=8 VI B8?C.

I>:C A8AB5<8 :@>2V: =54>AB0B=VABL :VAB:>2>3><>7:C.

I>:C =5@2>2>W A8AB5<8: A540B82=89 5D5:B, ?>3V@H5==O ?0<□OBV.

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

I>:C VW A8AB5<8: <548:0<5=B>7=5 28A8?0==O 7 5>78=>DV;VTN B0 A8AB5<=8<8 A8<0<8 (DRESS).

I>:C H:V@8: 3>AB@89 35=5@0;V7>20=89 5:70=B5<0B>7=89 ?CABC;L>7 (AGEP), ;VE5=>W4=89 :5@0B>7, >=VE><0457.

I>:C :VAB:>2>-< O7>2>W A8AB5<8: ?5@5;><8.

01>@0B>@=V ?>:07=8:8: 7=865==O W IV;L=>ABV :VAB:>2>W B:0=8=8.

5@54>7C20==O.

!8<8:

7 I>:C F5=B@0;L=>W =5@2>2>W A8AB5<8: ?@83=VG5==O DC=:FV9 &! , 457>@VT=B0FVO, ?@83=VG5=89 @V25=L A2V4<>ABV, A>=:82VABL, 71C465==O, 30;NF8=0FVW, :>0, 70BC<0=5==O 7>@C, =5@>71V@;820 <>20, 4870@B@VO, =VAB03<, 0B0:AVO, 48A:V=57VO, 3V?5@@5D;5:AVO (A?>G0B:C), 3V?>@5D;5:AVO (?V7=VH5), AC4<8, ?A8E<>B>@=V @>7;048, :;>=CA, 3V?>B5@

7 I>:C 48E0;L=>W A8AB5<8: ?@83=VG5==O 48E0==O, =01@O: ;535=V2;

7 I>:C A5@F52>-AC48==>W A8AB5<8: B0EV:0@4VO, 0@B5@V0;L=0 3V?>B5=7VO, V=>4V 0@B5@V0;L=0 3V?5@B5=7VO, ?>@CH5==O ?@>2V4=>ABV 7 @>7H8@5==O< :>?5, 72O70=5 7 7C?8=:>N A5@FO, I> AC?@>2>46CTBLAO 2B@0B>N A2V4<>ABV;

7 I>:C B@02=>3> B@0:BC: 1;N20==O, 70B@8

7 I>:C :VAB:>2>-<O7>2>W A8AB5<8: ?>2V4<<O;>AO ?@> :@5;V7C, ?>2O70=>3> 7 B>:A8G=8< 2?;82< :0@10<075?V=C;

7 I>:C A5G>284V;L=>W A8AB5<8: 70B@8;V3C@VO 01> 0=C@VO; 70B@8 0=B84VC@5B8G=>3> 3>@ <>=C;

;01>@0B>@=V ?>:07=8:8: 3V?>=0B@VT

V:C20==O. !?5F8DVG=89 0=B84>B 2V4ACB=V9. !?>G0B:C ;V:C20==O ?>28==> '@C=BC20B8AO =0 ;V=VG=>@>3>; ?>:070=0 3>A?VB0;V70FVO. @>2>48BLAO 287=0G5==O :>=F5=B@0FVW :0@10 <075?V=C C ?;072V 4;O ?V4B25@465==O >B@CT==O F8< 70A>1<< B0 >FV=:8 ABC?5=O ?5@54>7C20==O.

@><820==O H;C=:0, 70AB>AC20==O 0:B82>20=>3> 2C3V;;O. V7=O 520:C0FVO H;C=:>2>3> 2:A8:0FVW C ?5@V>4 >4C60==O. 0AB>A>2CTBLAO A8<0B8G=5 ?V4B@8W B5@0?VW, <=VB>@8=3 DC=:FV9 A5@FO, :>@5:FVO 5;5:B@>;VB=8E @>7;04V2.

A>1;82V @5:><5=40FVW. @8 @>728B:C 0@B5@V0;L=>W 3V?>B5=7VW ?>:070=5

2=CB@VH=L>25==5 22545==O 4>?0 4>1CB0728B:C ?>@CH5=L @8B; ?@8 @>728B:C AC4< 22545==O
15=7>4V075?V=V2 (=0?@8:;04 4V075?0 V=H8E ?@>B8AC4<=8E 70A>1V2, =0?@8:;04 D5=>10@1VB0;C
(7 >15@56=VABN G5@57 ?V428I5=89 @878: @>728B:C ?@83=VG5==O 48E0==O) 01> ?0@0;L453V4C;
?@8 @>728B:C 3V?>=0B@VT4=>W V=B>:A8:0FVW) >1<565==O 22545==O @V48=8, ?>2V;L=0
2=CB@VH=L>25==0 V=DC7VO 0,9 % @>7G8=C =0B@VN E;>@84C. &V 70E>48 <>6CBL 70?>1V3B8
=01@O:C <>7:C.

5:>5=4CTBLAO ?@>2545==O 35<>A>@1FVW =0 2C3V;L=8E A>@15=B0E. >2V4<;O;>AO ?@>
=55D5:B82=VABL D>@A>20=>3> 4VC@57C V ?5@8B>=50;L=>3> 4V0;V7C.

5>1EV4=> ?5@5410G8B8 <>6;82VABL ?>2B>@=>3> ?>A8;5==O A87C20==O =0 2-9 V 3-9 45=L, I> 7C
<>2;5=> C?>2V;L=5=8< 2A<:BC20==O< ?@5?0@0BC.

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

B20@8= ?5@>@0;L=5 70AB>AC20==O :0@10<075?V=C A?@8G8=O;> @>728B>: 45D5:BV2.
4VB59, <0B5@V O:8E AB@0640NBL =0 5?V;5?AVN, 2V47=0G0TBLAO AE8;L=VABL 4> ?>@CH5=L
2=CB@VH=L>CB@>1=>3> @>728B:C, C B>465=8E 204 @>728B:C. >2V4<;O;>AO ?@> V
<>2V@=VABL B>3>, I> :0@10<075?V=, O: V 1V;LHVABL ?@>B85?V;5?B8G=8E 70A>1V2, ?V428ICT
G0AB>BC B0:8E ?>@CH5=L, >4=0: ?5@5:>=;82V 4>:078 C @0=B@>;L>20=8E 4>A;V465=L
<=>B5@0?VW :0@10<075?V=>< 2V4ACB=V. 07< 7 B8< ?>2V4<;O;>AO ?@> 0A>FV9>20=V V7
70AB>AC20==O< :0@10<075?V=C ?>@CH5==O 2=CB@VH=L>CB@>1=>3> @>728B:C B0 2@>465=V
2048 @>728B:C, C B> IV;8=C E@51B0 B0 V=HV 2@>465=V 0=><0;VW, =0?@8:;04; I5;5?=>-;8FL>2V
45D5:B8, :0@4V>20A:C;O@=V 2048 @>728B:C, 3V?>A?04VO B0 0=><0;VW @>728B:C @V7=8E A8AB5
<>@30=V7

!;V4 27OB8 4> C2038 B0:V @5:><5=40FVW.

0AB>AC20==O ?@5?0@0BC 0@10<075?V=□AB@0D0@< 203VB=8<, E2>@8< =0 5?V;5?AVN
?>B@51CT >A>1;82>W C2038.

/:I> 6V=:0, O:0 >B@8

V=:0< @5?@>4C:B82=>3> 2V:C ?> <>6;82>ABV :0@10<075?V= A;V4 ?@87=0G0B8 O: <=>B5@0?VN.
5:>5=4CTBLAO ?@87=0G0B8 2V.

0FVT=B>: ?>B@V1=> ?>V=D>@ ?V428I5=89 @878: @>728B:C 2@>465=8E 204 C 4VB59 B0 A;V4
=04020B8 W< <>6;82VABL 0=B5=0B0;L=>3> A:@8=V=3C.

?5@V>4 203VB=>ABV =5 A;V4 ?5@5@820B8 5D5:B82=C ?@>B85?V;5?B8G=C B5@0?VN, >A:V;L:8
703>AB@5==O 70E2>@N20==O 703@>6C20B8<5 74>@>2N O: <0B5@V, B0: V 48B8=8.

!/?>AB5@565==O B0 ?@>DV;0:B8:0. □V4<>, I> C ?5@V>4 203VB=>ABV <>6;8289 @>728B>:
=54>AB0B=>ABV D>;VT2>W :8A;>B8. @>B85?V;5?B8G=V ?@5?0@0B8 <>6CBL ?V428IC20B8 @V25=L
=54>AB0B=>ABV D>;VT2>W :8A;>B8, B><5=4CTBLAO 4>40B:>25 ?@87=0G5==O D>;VT2>W :8A;>B8
4> 203VB=>ABV B0 C ?5@V>4 203VB=>ABV.

>2>=0@>465=V. <5B>N ?@>DV;0:B8:8 ?>@CH5=L 73>@B0==O :@>2V C =>2>=0@>465=8E @5:>
<5=4>20=> ?@87=0G0B8 2VB0< <0B5@O< ?@>BO3<< >AB0==VE B86=V2 203VB=>ABV B0
=>2>=0@>465=8

V4<< B0/01> ?@83=VG5==O 48E0==O C =>2>=0@>465=8E, :V;L:0 28?04:V2 1;N20==O, 4V0@5W B0
/01> ?>30=>3> 0?5B8BC C =>2>=0@>465=8E, I> ?>2O7CNBL V7 ?@89<<< :0@10<075?V=C B0 V=H8E
?@>B8AC4<=8E ?@5?0@0BV2.

>4C20==O 3@C44N. □0@10<075?V= ?@>=8:0T C 3@C4=5 <>;> (25-60 % :>=F5=B@0FVW C ?;072V).
5@52038 3>4C20==O 3@C44N B0 V<>2V@=VABL @>728B:C ?>1VG=8E 5D5:BV2 C =5<>2;OB8 A;V4
@5B5;L=> 72068B8. 0B5@V, O:V >B@8W A>=;82>ABV, 0;5@3VG=8E H:V@=8E @50:FV9).

\$5@B8;L=VABL.

C65 @V4:> ?>2V4<;O;>AO ?@> 28?04:8 ?>@CH5==O D5@B8;L=>ABV C G>;>2V:V2 B0/01> ?@>
2V4E8;5==O 2V4 =>@<8 ?>:07=8:V2 A?5@<0B>35=57C.

VB8.

VBO< 7 >3;O4C =0 1V;LH H284:C 5;V

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

0@10<075?V=-□AB@0D0@< A;V4 70AB>A>2C20B8 ;8H5 ?V4 <548G=8< =03;O4><, ?VA;O >FV=:8
A?V22V4=>H5=O :>@8ABL/@878: B0 70 C<>28 @5B5;L=>3> <=>VB>@8=3C AB0=C ?0FVT=BV2 C
@07V A5@F528E, ?5GV=:>28E 01> =8@:>28E ?>@CH5=L, ?>1VG=8E 35<0B>;>3VG=8E @50:FV9 =0
V=HV ?@5?0@0B8 2 0=0<=57V B0 C @07V ?5@5@20=>3> :C@AC B5@0?VW :0@10<075?V=>
5:>5=4CTBLAO ?@>2545==O 7030;L=>3> 0=0;V7C A5GV B0 287=0G5==O @V2=O 07>BC A5G>28=8 2
:@>2V =0 ?>G0B:C V 7 ?52=>N ?5@V>48G=VABN ?V4 G0A B5@0?VW.

0@10<075?V= ?@>O2;OT ;53:C 0=B8E>;V=5@3VG=C 0:B82=VABL, B>
!;V4 ?0<OB0B8 ?@> <>6;82C 0:B820FVN ?@8E>20=8E ?A8E>7V2, 0 I>4> ?0FVT=BV2 ;VB=L>3> 2V:C
?@> <>6;82C 0:B820FVN A?;CB0=>ABV A2V4<>ABV B0 B@82>6=5 71C465==O.

@5?0@0B 70728G09 =55D5:B82=89 ?@8 01A0=A0E (<0;8E 5?V;5?B8G=8E =0?040E) B0 ;>=VG=8E
=0?040E. :@5 B5, I> ?>A8;5==O =0?04V2 <>6;825 C ?0FVT=BV2 7 0B8?>28<8 01A0=A0<8.

5<0B>;>3VG=V 5D5:B8. 7 70AB>AC20==O< ?@5?0@0BC ?>2O7CNBL @>728B>: 03@0=C;>F8B>7C B0
0?;0AB8G=>W 0=54=0: G5@57 =04728G09=> =87L:C G0AB>BC 28?04:V2 @>728B:C F8E AB0=V2 206:>
>FV=8B8 7=0GCIVABL @878:C. 030;L=89 @878: @>728B:C 03@0=C;>F8B>7C 4;O E2>@8E, O:V =5
>B@828BL 4,7 >A>18/1000000 =0 @V.;, @>728B:C 0?;0AB8G=>W 0=5>A>18/1000000 =0 @V:.

0FVT=BV2 ?>B@V1=> ?>V=D>@ @0==V >7=0:8 B>:A8G=>ABV B0 A8<8 <>6;828E 35<0B>;>3VG=8E
?>@CH5=L, 0 B0:>6 ?@> A8<8 45@<0B>;>3VG=8E B0 ?5GV=:>28E @50:FV9. 0FVT=B0 A;V4
?>?5@548B8, I> C @07V ?>O28 B0:8E @50:FV9, O: 60@, 0=3V=0, H:V@=V 28A8?0==O, 28@07:8 C
@>B>2V9 ?>@>6=8=V, A8=FV, O:V ;53:> 28=8:0NBL, B>G:>2V :@>2>28;828 01> 35<>@03VG=0
?C@?C@0, A;V4 =5309=> 725@=CB8AO 4> ;V:0@O.

/:I> :V;L:VABL ;59:>F8BV2 01> B@>1>F8BV2 7=0G=> 7=86CTBLAO ?V4 G0A B5@0?VW, ?>B@V15=
@5B5;L=89 <=>VB>@8=3 AB0=C ?0FVT=B0, 7>:@5<0 ?>B@V1=> ?>ABV9=> @>18B8 7030;L=89
0=0;V7 :@>2V. V:C20==O ?@5?0@0B< 0@10<075?V=-□AB@0D0@< =5>1EV4=> ?@8?8=8B8, O:I> C
?0FVT=B0 @>72820TBLAO ;59:>?5=VO, O:0 T A5@9>7=>N, ?@>3@5ACNG>N 01> AC?@>2>46CTBLAO
;V=VG=8<8 ?@>O20<8, =0?@8;:04 30@OG:>N 01> 1>;5< C 3>@;V. 0AB>AC20==O ?@5?0@0BC 0@10
<075?V=-□AB@0D0@< A;V4 ?@8?8=8B8 ?@8 ?>O2V >7=0: ?@83=VG5==O DC=:FVW :VAB:>2>3>
<>7:C.

'0AB> 2V47=0G0TBLAO 7=865==O :V;L:>ABV B@>1>F8BV2 01> 1V;8E ;VB8= :@>2V C 7207:C 7
?@89><< ?@5?0@0BC 0@10<075?V=-□AB@0D0@ABV 28?04:V2 2>=> B825 V =5 A2V4G8BL ?@>
@>728B>: 0?;0AB8G=>W 0=5 03@0=C;>F8B>7C. > ?>G0B:C B5@0?VW B0 ?5@V>48G=> ?V4 G0A WW
?@>2545==O A;V4 @>18B8 0=0;V7 :@>2V, 2;;NG0NG8 287=0G5==O :V;L:>ABV B@>1>F8BV2 (0
B0:>6, <>6;82>, :V;L:>ABV @5B8:C;>F8BV2 B0 @V2=O 35<>3;>1V=C).

!5@9>7=V 45@<0B>;>3VG=V @50:FVW. !5@9>7=V 45@<0B>;>3VG=V @50:FVW, O:V 2;;NG0NBL
B>:A8G=89 5?V45@<0;L=89 =5:@>;V7 (")01> A8=4@>09T;;0, B0 A8=4@> !BV25=A0-6=>A>=0 (!),
?@8 70AB>AC20==V ?@5?0@0BC 0@10<075?V=-□AB@0D0@< 28=8:0NBL 4C65 @V4:>. 0FVT=B8 7
A5@9>7=8<8 45@<0B>;>3VG=8<8 @50:FVO<8 <>6CBL ?>B@51C20B8 3>A?VB0;V70FVW, >A:V;L:8 FV
AB0=8 <>6CBL 703@>6C20B8 68BBN. V;LHVABL 28?04:V2 @>728B:C !!/"2V47=0G0NBLAO ?@>BO3>
< ?5@H8E :V;L:>E 728B:C A8 A2V4G0BL ?@> A5@9>7=V 45@<0B>;>3VG=V @50:FVW (=0?@8;:04 !!,
A8=4@>> 09T;;0/"), ?@89> ?@5?0@0BC A;V4 =5309=> ?@8?8=8B8 B0 ?@87=0G8B8 0;LB5@=0B82=C
B5@0?VN.

\$0@<0:>35=>

O2;OTBLAO 2A5 1V;LH5 A2V4G5=L ?@> 2?;82 @V7=8E 0;5;V2 HLA =0 AE8;L=VABL ?0FVT=B0 4>
28=8:=5==O ?>1VG=8E @50:FVW, ?>2O70=8E 7 VN A8AB5<>N.

207>: V7 (HLA)-*1502

>A;V465==O 70 CG0ABN ?0FVT=BV2-:8B09FV2 5B=VG=>W 3@C?8 E0= ?@>45<=>=AB@C20;8
28@065=C :>@5;OFVN (HLA)-*1502. V;L:VABL =>AVW2 FL>3> 0;5;O A5@54 =0A5;5==O
7VW AB0=>28BL ?>=04 15 % =0 \$V;V??V=0E, C "0W;0=4V, >=:>=3C B0 0;097VW,
?@81;87=> 10 % C "0920=V, <0965 4 % C V2=VG=> 2V4 2 % 4> 4 % C V245==V9 7VW
(2;;NG0NG8 =4VN) V <5=H5 1 % C /?>=VW B0 >@5W. >H8@5==O 0;5;O (HLA)-*1502
T =57=0G=8< A5@54 T2@>?59AL:8E, 0D@8:0=AL:8E =0@>4V2, A5@54 :>@V==>3>
=0A5;5==O <5@8:8 B0 ;0B8=>0<5@8:0=AL:>3> =0A5;5==O.

B8E ?0FVT=BV2, O:V 35=5B8G=> =0;560BL 4> 3@C? @878:C, ?5@54 ?>G0B:>;V:C20==O
?@5?0@0B< 0@10<075?V=-□AB@0D0@< A;V4 ?@>2>48B8 B5ABC20==O =0 ?@8ACB=VABL 0;5;O
(HLA)-*1502. /:I> 0=0;V7 ?0FVT=B0 =0 ?@8ACB=VABL 0;5;O (HLA)-*1502 40T ?>78B82=89 @57C;LB0B,
B> ;V:C20==O ?@5?0@0B< 0@10<075?V=-□AB@0D0@< @>7?>G8=0B8 =5 A;V4, >:@V< 28?04:V2,

>:8 2V4ACB=V V=HV 20@V0=B8 B5@0?52B8G=>3> ;V:C20==O. 0FVT=B8, O:V ?@>9H;8 >1AB565==O
B0 >B@8<0;8 =530B82=89 @57C;LB0B I>4> (HLA)-B*1502, <0NBL =87L:89 @878: @>728B:C !!.
0 F59 G0A B>G=> =52V4<>, G8 2AV ?0FVT=B8 ?>E>465==O< 7 V245==>-!EV4=>W 7VW <0NBL F59
@878:.
002=VABL 0;5;O (HLA)-*1502 T D0:B>@< @878:C @>728B:C !!/"C ?0FVT=BV2:-8B09FV2, O:V >B@8
B85?V;5?B8G=V 70A>18, I> <>6CBL A?@8G8=OB8 28=8:=5==O !!/" . "0:8< G8=><, A;V4 C=8:0B8
70AB>AC20==O V=H8E ?@5?0@0BV2, I> <>6CBL A?@8G8=OB8 28=8:=5==O !!/" , ?0FVT=B0<, O:V
<0NBL 0;5;L (HLA)-*1502, O:I> <>6=0 70AB>A>2C20B8 V=HC B5@0?VN. 0728G09 =5 ?>B@V1=>
?@>2>48B8 35=5B8G=89 A:@8=V=3 ?0FVT=BV2 B8E =0FV>=0;L=>AB59, C ?@54AB02=8:V2 O:8E
=87L:89 :>5DV FVT=B 0;5;O (HLA)-*1502. 0728G09 =5 ?@>2>4OBL A:@8=V=3 E2>@8E, O:V 265 >B@8
?0FVT=BV2 T2@>?5>W4=>W @0A8 7207>:
207>: V7 HLA-*3101
59:>F8B0@=89 0=B835= ;N48=8 T D0:B>@< @878:C @>728B:C H:V@=8E ?>1VG=8E @50:FV9, B0:8E
O: !!, ", <548:0<5=B>7=89 28A8? 7 5>78=>DV;VTN B0 A8AB5<=8<8 A8<0<8 (DRESS), 3>AB@89
35=5@0;V7>20=89 5:70=B5<0B>7=89 ?CABC;L>7 (AGEP), <0:C;>?0?C;L>7=89 28A8?. /:I> 0=0;V7
2802;OT =002=VABL 0;5;O HLA-*3101, B> 2V4 70AB>AC20==O ?@5?0@0BC 0@10<075?V=-□
AB@0D0@< A;V4 CB@8<0B8AO.
=HV D0:B>@8
@V< 35=5B8G=>3> A:@8=V=3C ?>B@V15= 2V4?>2V4=89 ;;V=VG=89 =03;O4 B0 ;V:C20==O
?0FVT=BV2. "O6:V H:V@=V ?>1VG=V @50:FVW <>6CBL A?@8G8=8B8 9 V=HV D0:B>@8, B0:V O:
=52V4?>2V4=5 4>7C20==O ?@>B85?V;5?B8G=>3> 70A>1C, =54>B@8<0==O @568@N20=L =5 282G0;8.
=HV 45@<0B>;>3VG=V @50:FVW.
>6;8289 B0:>6 @>728B>: A:>@<8=C18E B0 ;53:8E 45@<0B>;>3VG=8E @50:FV9, =0?@8:;04
V7>;L>20=>W <0:C;O@=>W 01> <0:C;>?0?C;L>7=>W 5:70=B5<8. 0728G09 2>=8 <8=0NBL G5@57 :V;L:0
4=V2 01> B86=V2 O: ?@8 =577C20==V, B0: V ?VA;O 7=865==O 4>78 ?@5?0@0BC. A:V;L:8 @0==V
>7=0:8 1V;LH A5@9>7=8E 45@<0B>;>3VG=8E @50:FV9 1C20T 4C65 A:;04=> 2V4@V7=8B8 2V4 ;53:8E
A:>@<8=CG8E @50:FV9, ?0FVT=B ?>28=5= ?5@51C20B8 ?V4 ?8;L=8< =03;O4<<, I>1 =5309=>
?@8?8=8B8 70AB>AC20==O ?@5?0@0BC C @07V ?>3V@H5==O AB0=C.
002=VABL C ?0FVT=B0 0;5;O HLA-* 3101 ?>2070=V 7 28=8:=5==O< <5=H A5@9>7=8E =51060=8E
@50:FV9 7 1>:C H:V@8 =0 :0@10<075?V=, B0:8E O: A8=4@< 3V?5@GCB;82>ABV 4> ?@>B8AC4>
<=8E 70A>1V2 01> =57=0G=V 28A8?0==O (<0:C;>?0?C;L>7=V 28A8?0==O). 4=0: =5 1C;> 2AB0=>2;5=>,
I> =002=VABL (HLA)-*1502 A2V4G8BL ?@> @878: 28=8:=5==O 28I5707=0G5=8E H:V@=8E @50:FV9.
V?5@GCB;82VABL. □0@10<075?V= <>65 A?@>2>:C20B8 @>728B>: @50:FV9 3V?5@GCB;82>ABV,
2:;NG0NG8 <548:0<5=B>7=89 28A8? 7 5>78=>DV;VTN B0 A8AB5<=8<8 A8<0<8 (DRESS), <=>68==V
@50:FVW 3V?5@GCB;82>ABV ?>2V;L=>3> B8?C 7 30@OG:>N, 28A8?0==O<, 20A:C;VB<<, ;V?0BVTN,
?A524>;V<>N, 0@B@0;3VTN, ;59:>?5=VTN, 5>78=>DV;VTN, 35?0B>A?;5=<530;VTN, 7:0@4, B>2ABC
:8H:C).
002=VABL C ?0FVT=B0 0;5;O HLA-* 3101 ?>2070=> 7 28=8:=5==O< <5=H A5@9>7=8E =51060=8E
@50:FV9 =0 :0@10<075?V= 7 1>:C H:V@8, B0:8E O: A8=4@< 3V?5@GCB;82>ABV 4> ?@>B8AC4>
<=8E 70A>1V2 01> =57=0G=V 28A8?0==O (<0:C;>?0?C;L>7=V 28A8?0==O).
0FVT=BV2 7 @50:FV0<8 3V?5@GCB;82>ABV =0 :0@10<075?V= ?>B@V1=> ?@>V=D>@ B5, I>
?@81;87=> 25-30 % B0:8E ?0FVT=BV2 B0:>6 <>6CBL <0B8 @50:FVW 3V?5@GCB;82>ABV =0
>:A:0@1075?V= («"@8;5?B0;®»)).
@8 70AB>AC20==V :0@10<075?V=C B0 D5=VB>W=C <>6;8289 @>728B>: ?5@5E@5A=>W
3V?5@GCB;82>ABV.
030;<< ?@8 ?>O2V A8 2:07CNBL =0 3V?5@GCB;82VABL, 70AB>AC20==O ?@5?0@0BC 0@10<075?V=-□
AB@0D0@< A;V4 =5309=> ?@8?8=8B8.
0?048. □0@10<075?V=-□AB@0D0@< A;V4 70AB>A>2C20B8 7 >15@56=VABN ?0FVT=B0< 7V 7
V428I5==O G0AB>B8 =0?04V2 <>6;825 ?V4 G0A ?5@5E>4C 2V4 ?5@>@0;L=8E D>@< :0@10<075?V=C
4> AC?>78B>@VW2.
\$C=:FVO ?5GV=:8. 5>1EV4=> ?@>2>48B8 >FV=:C DC=:FVW ?5GV=:8 =0 ?>G0B:C B0 ?5@V>48G=>
?@>BO3<< B5@0?VW, >A>1;82> C ?0FVT=BV2 V7 70E2>@N20==O<8 ?5GV=:8 2 0=0<=57V B0 C
?0FVT=BV2 ;VB=L>3> 2V:C. @8 703>AB@5==V ?>@CH5=L DC=:FVW ?5GV=:8 =5>1EV4=> =5309=>
?@8?8=8B8 ?@89<< ?@5?0@0BC.

50:V ?>:07=8:8 ;01>@0B>@=8E 0=0;V7V2, 70 4>?<>3>N O:8E >FV=NNBL DC=:FV>=0;L=89 AB0=
?5GV=:8, C ?0FVT=V2, O:V ?@89<0NBL :0@10<075?V=, <>6CBL 28E>48B8 70 <56V =>@<8, 7>:@5<0
@V25=L 30<<0-3;CB03> ?V428I5==O @V2=O ;C6=>W D>AD0B078. "0:5 ?V428I5==O DC=:FV>=0;L=>W
0:B82=>ABV ?5GV=:>2>3> <5B01>;V7:070==O< 4;O 2V4

"O6:V @50:FVW 7 1>:C ?5GV=:8 G5@57 70AB>AC20==O :0@10<075?V=C A?>AB5@V30NBLAO 4C65
@V4>: # @07V 28=8:=5==O A82>W 48ADC=:FVW 01> 0:B82=>3> 70E2>@N20==O ?5GV=:8 =5>1EV4=>
B5@2> >1AB568B8 ?0FVT=B0, 0 ;V:C20==O ?@5?0@0B< 0@10<075?V=- □AB@0D0@< ?@87C?8=8B8
4> >B@8<0==O @57C;LB0BV2 >1AB565==O.

\$C=:FVO =8@>.: 5:><5=4CTBLAO ?@>2>48B8 >FV=:C DC=:FVW =8@>: B0 287=0G5==O @V2=O
07>BC A5G>28=8 :@>2V =0 ?>G0B:C B0 ?5@V>48G=> ?@>BO3< :C@AC B5@0?VW.

V?>=0B@VT□V4>728B:C 3V?>=0B@VTAC20==V :0@10<075?V=C. # ?0FVT=V2 7 ?>@CH5==O<
DC=:FVW =8@>:, O:5 ?>2O70=> 7V 7=865=8< @V2=5< =0B@VN, 0 B0:>6 C @07V AC?CB=L>3>
;V:C20==O 70A>10<8, O:V 7=86CNBL @V25=L =0B@VN (B0:8<8 O: 4VC@5B8:8, ;V:0@AL:V 70A>18, I>
0A>FVNNBLAO 7 =5045:20B=>N A5:@5FVTN 0=B84VC@5B8G=>3> 3>@<>=C), ?5@54 ;V:C20==O<
A;V4 282V. 0;V A;V4 286=V 2 B86=V, ?>BV< 7 V=B5@20;< 2 1 BO3<< ?5@H8E 3 70 ;;V=VG=>N
=5>1EV4=VABN. &5 AB>ACTBLAO C ?5@HC G5@3C ?0FVT=V2 ;VB=L>3> 2V:C. # B0:>1<56C20B8
26820==O 2>48.

V?>B8@5>W487□0@10<075?V= <>65 7=86C20B8 :>=F5=B@0FVN 3>@<>=V2 I8B>284=>W 70;>78 C
7207:C 7 F8< =5>1EV4=5 71V;LH5==O 4>78 70W B5@0?VW 3>@<>=0<8 I8B>284=>W 70;>78 4;O
?0FVT=V2 7 3V?>B8@5>W487<>

=B8E>;V=5@3VG=V 5D5:B8. □0@10<075?V= ?@>O2;OT ?>;V=5@3VG=C 0:B82=VABL. "0:8< G8=><,
?0FVT=B8 7 ?V428I5=8< 2=CB@VH=L>>G=8< B8A:>< B0 70B@8N A5GV ?>28==V ?5@51C20B8 ?V4
?8;L=8< =03;O4<< ?V4 G0A B5@0?VW.

A8EVG=V 5D5:B8. !;V4 ?0<OB0B8 ?@> V<>2V@=VABL 0:B82V70FVW ;0B5=B=>3> ?A8E>7C, C
?0FVT=V2 ;VB=L>3> 2V:C A?;CB0=>ABV A2V4<>ABV 01> 71C465=>ABV.

!CWF840;L=V 4C254V=:0. C;> 70@5TAB@>20=V :V;L:0 A2V4G5=L ?@> ACWF840;L=V 4Q254V=:C C
?0FVT=V2, O:V >B@8B85?V;5?B8G=V ?@5?0@0B8. 5B00=0;V7 40=8E, >B@8<0=8E C E>4V
4>A;V465=L ?@>B85?V;5?B8G=8E ?@5?0@0BV2, B0:>6 ?>:0702 =525;8:5 ?V428I5==O @878:C ?>O28
ACWF840;L=8E 4C<>: V ?>254V=:8. 5E0=V7< 28=8:=5==O B0:>3> @878:C =52V4<<89, 0 4>ABC?=V
40=V =5 28;;NG0NBL ?V428I5==O @878:C ACWF840;L=8E 4C<>: V ?>254V=:8 ?VA;O 70AB>AC20==O
:0@10<075?V=C.

">1EV4=> ?5@52V@8B8 =0 =0O2=VABL ACWF840;L=8E 4C<>: B0 ?>254V=:8 V, O:I> ?>B@V1=>,
?@87=0G8B8 2V4?>2V4=5 ;V:C20==O. 0FVT=B0< (B0 >A>10<, O:V 4>3;O40NBL 70 ?0FVT=B0<8) A;V4
@5:><5=4C20B8 725@=CB8AO 4> ;V:0@O C @07V ?>O28 >7=0: ACWF840;L=8E 4C<>: B0 ?>254V=:8.
=4>:@8==V 5D5:B8. '5@57 V=4C:FVN D5@<5=V2 ?5GV=:8 :0@10<075?V= <>65 AB0B8 ?@8G8=>N
7=865==O B5@0?52B8G=>3> 5D5:BC ?@5?0@0BV2 5AB@>35=V2 B0 ?@>35AB5@>=C. &5 <>65
?@8725AB8 4> 7=865==O 5D5:B82=>ABV :>=B@0F5?FVW, @5F8482C A8?@>@82=8E :@>2>B5G B0
:@>2O=8E 284V;5=L. 0FVT=B:8, O:V ?@89<0NBL 0@10<075?V=- □AB@0D0@< V 4;O O:8E 3>@
<>=0;L=0 :>=B@0F5?FVO T =5>1EV4=>N, ?>28==V >B@8 35=C. V=H>: A;V4 @>73;O=CB8 <>6;82VABL
28:>@8AB0==O 0;LB5@=0B82=8E =53>@<>=0;L=8E <5B>4V2 :>=B@0F5?FVW.

>=VB>@8=3 @V2=O ?@5?0@0BC C ?;072V. 572060NG8 =0 B5, I> :>@5;OFVO 70<8 B0 @V2=5< :0@10
<075?V=C C ?;072V, 0 B0:>6 2V B0 ;;V=VG=>N 5D5:B82=VABN V ?5@5=>A82;5=0, <=>VB>@8=3
@V2=O ?@5?0@0BC C ?;072V <>65 1CB8 4>FV;L=8< C B0:8E 28?04:0E: ?@8 @0?B>2>B8 =0?04V2,
?5@52V@FV :>4 203VB=>ABV, C @07V ;V:C20==O 4VB59 B0 ?V4;VB:V2; ?@8 ?V4>7@V =0
?>@CH5==O 01A>@1FVW, ?@8 ?V4>7@N20=V9 B>:A8G=>ABV B0 ?@8 70AB>AC20==V 1V;LH5
>4=>3> ?@5?0@0BC.

=865==O 4>78 B0 2V4 0?B>20 2V4

=865==O 4>78 B0 A8=4@<< 2V4 0?B>20 2V4ABC?>2> ?@>BO3<< 6 1EV4=>ABV =5309=>W 2V4

**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.**

40B=VABL ?0FVT=B0, O:89 ?@89<0T 0@10<075?V=- □AB@0D0@<, 4> H284:>W @50:FVW <>65 1CB8
?>@CH5=0 (>A>1;82> =0 ?>G0B:C B5@0?VW 01> C ?5@V>4 ?V41>@C 4>78) 2=0A;V4>: 28=8:=5==O
70?0<>@>G5==O V A>;82>ABV, B<>1V;5< 01> @>1>BV 7 V=H8<8 <5E0=V7<0<8 ?0FVT=BC A;V4
1CB8 >15@56=8

70T<>4V0 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9.

&8B>E@<< 450 34 (CYP3A4) T >A=>2=8< D5@<5=B<<, I> :0B0;V7CT CB2>@5==O 0:B82=>3>
<5B01>;VBC :0@10<075?V=C-10,11-5?>:A84C. 4=>G0A=5 70AB>AC20==O V=3V1VB>@V2 CYP3A4
<>65 A?@8G8=OB8 ?V428I5==O :>=F5=B@0FVW :0@10<075?V=C C ?;072V, I>, C A2>N G5@3C, <>65
?@872>48B8 4> @>728B:C ?>1VG=8E @50:FV9. 4=>G0A=5 70AB>AC20==O V=4C:B>@V2 CYP3A4
<>65 ?>A8;N20B8 <5B01>;V7< :0@10<075?V=C, I> ?@872>48BL 4> 7=865==O :>=F5=B@0FVW :0@10
<075?V=C C A8@>20BFV :@>2V B0 ?>A;01;5==O B5@0?52B8G=>3> 5D5:BC. >4V1=8< G8=><
?@8?8=5==O ?@89>@0 CYP3A4 <>65 7=86C20B8 H284:VABL<5B01>;V72V.
0@10<075?V= T ?>BC6=8< V=4C:B>@<< CYP3A4 B0 V=H8E D5@<5=B=8E A8AB5< D078 B0 D078 C
?5GV=FV, B>2V V=H8E ?@5?0@0BV2, O:V ?5@5206=> <5B01>;V7CNBLAO CYP3A4 H;OE<<
V=4C:FVW WE=L>3> <5B01>;V7
N4AL:0 A><0;L=0 5?>:A84-3V4@>;070 O2;OT A>1>N D5@<5=B, 2V4?>2V40;L=89 70 CB2>@5==O 10,11-
B@0=A4V>;?>EV4=8E :0@10<075?V=C-10,11-5?>:A84C. 4=>G0A=5 70AB>AC20==O V=3V1VB>@V2
;N4AL:>W A><0;L=>W 5?>:A84-3V4@>;078 <>65 ?@8725AB8 4> ?V428I5==O :>=F5=B@0FV9 :0@10
<075?V=C-10,11-5?>:A84C C ?;072V.
@5?0@0B8, O:V <>6CBL ?V428IC20B8 @V25=L :0@10<075?V=C C ?;072V.
A:V;L:8 ?V428I5==O @V2=O :0@10<075?V=C C ?;072V <>65 ?@872>48B8 4> ?>O28 =51060=8E
@50:FV9 (B0:8E O: 70?0<>@>G5==O, A>=;82VABL, 0B0:AVO, 48?;>?VO), B> 4>7C20==O ?@5?0@0BC
0@10<075?V=-□AB@0D0@< =5>1EV4=> 2V4?>2V4=> :>@83C20B8 B0/01> :>=B@>;N20B8 9>3>
@V2=V C ?;072V ?@8 >4=>G0A=>AC20==V 7 =86G5707=0G5=8<8 ?@5?0@0B0<8.
=0;35B8:8, ?@>B870?0;L=V ?@5?0@0B8: 45:AB@>?@>?>:A8D5=, V1C?@>D5=
=4@>35=8: 40=07>;.
=B81V>B8:8: <0:@>;V4=V 0=B81V>B8:8 (=0?@8;:04 5@8B@>;50=4>70D;>:A0F8=).
=B845?@5A0=B8: 4578?@0:A5B8=, D;C2>:A04>=, ?0@>:A5B8=, B@07>4>=, 2V;>:A078=
@>B85?V;5?B8G=V 70A>18: AB8@8?5=B>;, 2V3010B@8=
@>B83@81:>2V 70A>18: 07>;8 (=0?@8;:04 VB@0:>=07>;, :5B>:>=07>;, D;C:>=07>;, 2>@8:>=07>;).
0FVT=B0<, O:V >B@8@8:>=07>;<< 01> VB@0:>=07>;<<, <>6=0 @5:><5=4C20B8 0;LB5@=0B82=V
?@>B85?V;5?B8G=V 70A>18.
=B83VAB0; >@0B048=, B5@D5=048=
=B8?A8E>B8G=V ?@5?0@0B8: >;0=70?V=, ;>:A0?V=, :25BV0?V=
@>B8BC15@:C:L>7=V ?@5?0@0B8: V7>=V0784.
@>B82V@CA=V ?@5?0@0B8: V=3V1VB>@8 ?@>B5078 4;O ;V:C20==O (=0?@8;:04 @8B>=02V@).
=3V1VB>@8 :0@1>0=3V4@078: 0F5B07>;0
!5@F52>-AC48==V ;V:0@AL:V 70A>18: 48;BV075<, 25@0?0
@5?0@0B8 4;O ;V:C20==O 70E2>@N20=L B@02=>3> B@0:BC: F8<5B848=, ><5?@07>;.
V>@5;0:A0=B8: >:A81CB8=V=, 40=B@>;5=
=B803@530=B=V 70A>18: B8;:>?V48=
=HV @5G>28=8: 3@59?D@CB>289 AV.; =V:>B8=@>A;8E, BV;L:8 C 28A>:8E 4>70E).
@5?0@0B8, O:V <>6CBL ?V428IC20B8 @V25=L 0:B82=>3> <5B01>;VBC :0@10<075?V=C-10,11-
5?>:A84C C ?;072V.
A:V;L:8 ?V428I5=89 @V25=L 0:B82=>3> <5B01>;VBC :0@10<075?V=C-10,11-5?>:A84C C ?;072V <>65
A?@8G8=8B8 @>728B>: ?>1VG=8E @50:FV9 (=0?@8;:04 70?0<>@>G5==O, A>=;82VABL, 0B0:AVN,
48?;>?VN), 4>7C20==O ?@5?0@0BC 0@10<075?V=-□AB@0D0@< =5>1EV4=> 2V4?>2V4=>
:>@83C20B8 B0/01> :>=B@>;N20B8 @V25=L :0@10<075?V=C C ?;072V, O:I> 9>3> ?@89<0NBL
>4=>G0A=> 7 B0:8<8 ?@5?0@0B0<8, O: ;>:A0?V=, :25BV0?V=, ?@8=, ?@>301V4, 20;L?@>T20 :8A;>B0,
20;=>:B0
@5?0@0B8, O:V <>6CBL 7=86C20B8 @V25=L :0@10<075?V=C C ?;072V.
>65 1CB8 =5>1EV4=>N :>@5:FVO 4>78 ?@5?0@0BC 0@10<075?V=-□AB@0D0@< ?@8 >4=>G0A=>
AC20==V 7 =86G5707=0G5=8<8 ?@5?0@0B0<8.
@>B85?V;5?B8G=V ?@5?0@0B8: D5;10<0B, <5BAC:A8:A:0@1075?V=, D5=>10@1VB>=, D5=AC:A8W=
(I>1 C=8:=CB8 V=B>:A8:0FVW D5=VB>W=><< B0 AC1B5@0?52B8G=8E :>=F5=B@0FV9 :0@10
<075?V=C, @5:><5=4>20=> 2V4:>@53C20B8 :>=F5=B@0FVN D5=VB>W=C C ?;072V 4> 13 = B0
:;>=075?0< (E>G0 40=V I>4> =L>3> AC?5@5G;82V).
@>B8?CE:8==V ?@5?0@0B8: F8A?;0B8= 01> 4>:A>@C1VF8=.

@>B8BC15@:C;L>7=V ?@5?0@0B8: @8D0
@>=E>48;0B0B>@8 01> ?@>B80AB<0B8G=V ?@5?0@0B8: B5>DV;V=, 0DV;V=
5@<0B>;>3VG=V ?@5?0@0B8: V7>B@5B8=>W=
70T<>4VO 7 V=H8<8 @5G>28=0<8: ?@5?0@0B8, I> 1V9 (*Hypericum perforatum*).
5D;>EV= <>65 ?@>O2;OB8 0=B03>=VAB8G=V 2;0AB82>ABV I>4> ?@>B85?V;5?B8G=>3> 5D5:BC
:0@010<075?V=C. V4?>2V4=> 4>7C ?@5?0@0BC 0@10<075?V=-□AB@0D0@< =5>1EV4=>
2V4:>@83C20B8.
?>2V4<>;5==O, I> V7>B@5B8=>W= 74>ABC?=VABL B0/01> ;;V@5=A :0@10<075?V=C V :0@10
<075?V=C-10,11-5?>;A84C; =5>1EV4=> :>=B@>;N20B8 :>=F5=B@0FVW :0@10<075?V=C C ?;072V.
?;82 :0@10<075?V=C =0 @V25=L C ?;072V >4=>G0A=> ?@87=0G5=8E ?@5?0@0BV2.
0@10<075?V= <>65 7=86C20B8 @V25=L 45O:8E ?@5?0@0BV2 C ?;072V B0 7<5=HC20B8 01>
=V25;N20B8 WE 5D5:B8. >65 28=8:=CB8 =5>1EV4=VABL :>@5:FVW 4>78 =86G5=02545=8E
?@5?0@0BV2 2V4?>2V4=> 4> ;;V=VG=8E 28<>3.
=0;35B8:8. ?@>B870?0;L=V ?@5?0@0B8: 1C?@5=>@DV=, <5B04>=, ?0@0F5B0<>; (B@820;5
70AB>AC20==O :0@10<075?V=C 7 ?0@0F5B0<>;< (0F5B0D5=><) <>65 A?@8G8=OB8 @>728B>:
35?0B>B>;A8G=>ABV), D5=07>= (0=B8?V@8=), B@0<04>;.
=B81V>B8:8: 4>;A8F8;;V=, @8D01CB8=
=B8:>03C;O=B8: ?5@>@0;L=V 0=B8:>03C;O=B8 (=0?@8;;04 20@D0@8=, D5=?@>:>C<>=, 48:C<0@>; B0
0F5=>;C<0@>);.
=B845?@5A0=B8: 1C?@>?V>=, F8B0;>?@0<,
@>B81;N2>B=V 70A>18: 0?5@?VB0=B.
@>B85?V;5?B8G=V ?@5?0@0B8: ;;>1070<, ;;>=075?0<, 5B>AC:F8=, BV0301V=, B>?V@0<0B,
20;L?@>T20 :8A;>B0, 7>=VA02V4<>;O;>AL O: ?@> ?V428I5==O @V2=O D5=VB>W=C C ?;072V
2=0A;V4>: 4VW :0@10<075?V=C, B0: V ?@> 9>3> 7=865==O, 0 B0:>6 ?@> ?>>48=>;V 28?04:8
71V;LH5==O @V2=O <5D5=VB>W=C C ?;072V.
@>B83@81:>2V ?@5?0@0B8: VB@0:>=07>;, 2>@8:>=07>;, :5B>=07>;. 0FVT=B0<, O:V >B@8@8:>=07>;>
< 01> V=B@0:>=07>;<;<, <>6=0 @5:><5=4C20B8 0;LB5@=0B82=V ?@>B85?V;5?B8G=V 70A>18.
=B835;L: ?@078:20=B5;;, 0;L15=407>;.
@>B8?CE:8==V ?@5?0@0B8: V<0B8=V1, F8:>D>AD0;V
59@>;5?B8G=V ?@5?0@0B8: ;;>70?V=, 30;>?5@84>; B0 1@>;, >;0=70?V=, :25BV0?V=, @8A?5@84>=,
78?@0784>=, 0@8?V?@07>;, ?0;V?5@84>=.
@>B82V@CA=V ?@5?0@0B8: V=3V1VB>@8 ?@>B5078 4;O ;V:C20==O (=0?@8;;04 V=48=02V@,
@8B>=02V@, A0:2V=02V@).
=:AV>;VB8:8: 0;?@07>;0<, ;0
@>=E>48;0B0B>@8 01> ?@>B80AB<0B8G=V ?@5?0@0B8: B5>DV;V=
>=B@0F5?B82=V ?@5?0@0B8: 3>@<>=0;L=V :>=B@0F5?B828 (A;V4 @>73;O=CB8 <>6;82VABL
70AB>AC20==O 0;LB5@=0B82=8E 70E>4V2 :>=B@0F5?FVW).
!5@F52>-AC48==V ;V:0@AL:V 70A>18: 1;>;0B>@8 :0;LFVT28E :0=0;V2 (3@C?0 483V4@>?V@848=C),
=0?@8;;04 D5;>48?V=, VA@048?V=, 483>;A8=, EV=V48=, ?@>?@0=>;>;, A8<20AB0B8=,
0B>@20AB0B8=, ;>20AB0B8=, F5@820AB0B8=, V201@048=
>@B8:>AB5@>W48: (7>:@5<0 ?@54=V7>;>=, 45:A0<5B07>=).
0A>18, O:V 70AB>A>2CNBL 4;O ;V:C20==O 5@5:B8;L=>W 48ADC=:FVW: B040;0DV;.
45?@5A0=B8: F8:>;A?>@8=, 525@>;V;V;V
"8@5>W4=V ?@5?0@0B8: ;52>B8@>;A8=
70T<>4VO 7 V=H8<8 ?@5?0@0B0<8: ?@5?0@0B8, I> 35=8 B0/01> ?@>35AB5@>=8 (A;V4 @>73;O=CB8
0;LB5@=0B82=V <5B>48 :>=B@0F5?FVW); 1C?@5=>DV=, 35AB@8=>=, B81>;>=, B>@5
><IV=0FVW ?@5?0@0BV2, O:V 28<030NBL >:@5<>3> @>73;04C.
4=>G0A=5 70AB>AC20==O :0@10<075?V=C B0 ;525B8@0F5B0 B>;A8G=>ABV :0@10<075?V=C.
4=>G0A=5 70AB>AC20==O :0@10<075?V=C B0 V7>=V0784C <>65 ?@8725AB8 4> ?>A8;5==O
35?0B>B>;A8G=>ABV V7>=V0784C.
4=>G0A=5 70AB>AC20==O :0@10<075?V=C V ?@5?0@0BV2 ;VBN 01> <5B>;>?@06 :0@10<075?V=C
V =59@>;5?B8:V2 (30;>?5@84>;, BV>@84078=) <>65 ?@8725AB8 4> ?>A8;5==O ?>1VG=8E
=52@>;>3VG=8E 5D5:BV2 (C @07V 70AB>AC20==O :><1V=0FVW 7 =59@>;5?B8:0<8 =02VBL 70
B5@0?52B8G=8E @V2=V2 C ?;072V).

><1V=>20=0 B5@0?VO ?@5?0@0B>< 0@10<075?V=-□AB@0D0@< B0 450:8<8 4VC@5B8:0<8
(3V4@>E;>@>BV0784, DC@>A5
0@10<075?V= <>65 ?5@5H:>460B8 5D5:B0< =545?>;O@87C20;L=8E <07>28E @5;0:A0=BV2 (=0?@8:;04
?0=:C@>=VN). >65 28=8:=CB8 =5>1EV4=VABL ?V428I5==O 4>7 F8E ?@5?0@0BV2, 0 ?0FVT=B8
?>B@51CNBL @5B5;L=>3> <=>VB>@8=3C/AB0=C G5@57 <>6;82VABL H284H>3>, =V6 >GV:CTBLAO,
7025@H5==O =59@><07>2>W 1;:>:048.
0@10<075?V=, O: V V=HV ?A8E>B@>?>V ?@5?0@0B8, <>65 7=86C20B8 ?5@5=>A83>;N, B>3>;N.
@>B8?>:070=V :><1V=0FVW.

A:V;L:8 :0@10<075?V= AB@C:BC@=> 1;87L:89 4> B@8F8;;VG=8E 0=B845?@5A0=BV2, ?@5?0@0B =5
@5:><5=4>20=> 70AB>A>2C20B8 >4=>G0A=> 7 V=3V1VB>@0<8 <=>0:A84078 (); ?5@54 ?>G0B:><
70AB>AC20==O ?@5?0@0BC =5>1EV4=> ?@8?8=8B8 ?@89>< V=3V1VB>@C (I=>09<5=H5 70 2 B86=V
01> @0=VH5, O:I> 4>72>;ONBL ;:V=VG=V >1AB028=8).
?:82 =0 A5@>;>3VG=V 4>A;V465==O.

0@10<075?V= <>65 40B8 E81=>?>78B82=89 @57C;LB0B %-0=0;V7C (28A>:>5D5:B82=0 @V48==0 E@>
<0B>3@0DVO) 4;O 287=0G5==O :>=F5=B@0FVW ?5@D5=078=C.
0@10<075?V= B0 10,11-5?>:A84 <>6CBL 40B8 E81=>?>78B82=89 @57C;LB0B V;>3VG=>3> 0=0;V7C 70
<5B>48:>N ?>;O@87>20=>W D;C>@5AF5=FVW 4;O 287=0G5==O :>=F5=B@0FVW B@8F8;;VG=8E
0=B845?@5A0=BV2.

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

\$0@<0:>48=0 !?5:B@ 0:B82=>ABV :0@10<075?V=C O: ?@>B85?V;5?B8G=>3> ;V:0@AL:>3> 70A>1C
>E>?;NT: ?0@FV0;L=V =0?048 (?@>ABV V :>@8=>N 35=5@0;V70FVTN B0 157 =5W;
35=5@0;V7>20=V B>=V:>.:>=VG=V AC4<=>V =0?048, 0 B0:>6 :><1V=0FVW 2:070=8E B8?V2 =0?04V2.
5E0=V7< 4VW :0@10<075?V=C 70A>20=89 ;8H5 G0AB:>2>. 0@10<075?V= AB01V;V7CT <5<1@0=8
=04B> 71C465=8E =5@2>28E 2>;>:=, V=3V1CT 28=8:=5==O ?>2B>@=8E =59@>=0;L=8E @>7@O4V2 V
7=86CT A8=0?B8G=5 ?@>2545==O 71C46C20;L=8E V< <>6;82>, I> 3>;>2=8< <5E0=V7<< 4VW
?@5?0@0BC T 70?>1V30==O ?>2B>@=>@5==N =0B@V970;56=8E ?>B5=FV0;V2 4VW C
45?>;O@87>20=8E =59@>=0E H;OE<< 1;:>:048 =0B@VT28E :0=0;V2, O:0 70;568BL 2V4 B@820;>ABV
70AB>AC20==O B0 2>;LB06C.

=865==O 282V;L=5==O 3;CB0<0BC V AB01V;V70FVO<5<1@0= =59@>=V2 <>65 ?>OA=8B8
?@>B8AC4><=C 4VN ?@5?0@0BC, 0 0=B8<0=V0:0;L=89 5D5:B :0@10<075?V=C <>65 1CB8 7C<>2;5=89
?@83=VG5==O< <5B01>;V7?0@04@5=0;V=C.

:;V=VG=8E 4>A;V465==OE ?@8 70AB>AC20==V :0@10<075?V=C O: <=>B5@0?VW C ?0FVT=BV2 7
5?V;5?AVTN (>A>1;82> C 4VB59 V ?V4;VB:V2) 1C;0 2V47=0G5=0 ?A8E>B@>?>=0 4VO ?@5?0@0BC, O:0
G0AB:>2> ?@>O2;O;0AO ?>78B82=8< 2?;82< =0 A8<8 B@82>6=>ABV V 45?@5AVW, 0 B0:>6 7=865==O
< @>74@0B>20=>ABV B0 03@5A82=>ABV. 0 40=8<8 @O4C 4>A;V465=L, 2?;82 :0@10<075?V=C =0
:>3=VB82=C DC=:FVN V ?A8E>@=V ?>:07=8:8 70;5602 2V4 4>78 V 1C2 01> AC<=V2=8<, 01>
=530B82=8A;V465==OE 1C2 2V47=0G5=89 ?>78B82=89 2?;82 ?@5?0@0BC =0 ?>:07=8:8, I>
E0@0:B5@87CNBL C203C, 740B=VABL 4> =02G0==O V 70?0<OB>2C20==O.

/: =59@>B@>?>=89 70AVI 0@10<075?V=-□AB@0D0@< 5D5:B82=89 ?@8 450:8E =52@>;>3VG=8E
70E2>@N20==OE: =0?@8:;04, 2V= 70?>1V30T 1>;L>28< =0?040< ?@8 V4V>?0B8G=V9 V 2B>@8==V9
=52@0;3VW B@V9G0AB>3> =5@20. @V< B>3>, 0@10<075?V=-□AB@0D0@< 70AB>A>2CTBLAO 4;O
?>;53H5==O =59@>35==>3> 1>;N ?@8 @V7=8E AB0=0E, C B>BFV A?8==>3> <>7:C, ?>ABB@02
<0B8G=8E ?0@5AB57VOE V ?>AB35@?5B8G=V9 =52@0;3VW. @8 A8=4@>3>;L=>W 01AB8=5=FVW
:0@10<075?V= ?V428ICT ?>@V3 AC4<=>W 3>B>2=>ABV (O:89 ?@8 FL>
V4B25@465=>, I> O: ?A8E>B@>?>=89 70AVI :0@10<075?V= 5D5:B82=89 ?@8 0D5:B82=8E
?>@CH5==OE, 0 A0<5: 4;O ;V:C20==O 3>AB@8E <0=V0:0;L=8E AB0=V2, 4;O ?V4B@83> ;V:C20==O
1V?>;O@=8E 0D5:B82=8E (<0=V0:0;L=>-45?@5A82=8E) @>7;04V2 (O: <=>B5@0?VO, 0 B0:>6 C :>
<1V=0FVW 7 =59@>;5?B8G=8<8 70A>10<8, 0=B845?@5A0=B0<8 01> ?@5?0@0B0<8 ;VBN).

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

A<>:BC20==O. VA;O ?@89>: :0@10<075?V= 2A<>:BCTBLAO <0965 ?>2=VABN, E>G0 V 45I>
?>2V;L=>. VA;O @07>2>3> ?@89>W B01;5B:8 <0:A8<0;L=0 :>=F5=B@0FVO C ?;072V (!_{max})
4>AO30TBLAO G5@57 12 3>48=. 5 2V47=0G0TBLAO ;:V=VG=> 7=0GCI8E 2V4AB59 C ABC?5=V 2A
<>:BC20==O 0:B82=>W @5G>28=8 ?VA;O 70AB>AC20==O @V7=8E ;V:0@AL:8E D>@< :0@10
<075?V=C 4;O ?@89>. VA;O >4=>@07>2>3> ?@89>B01;5B:8 ?@5?0@0BC, I> !_{max} =57W 0:B82=>W

@5G>28=8 4>AO30T 1;87L:> 4,5
V>4>ABC?=VABL @V7=8E ;V:0@AL:8E D>@< :0@10<075?V=C 4;O ?5@>@0;L=>3> ?@89> ?>:070=>,
;568BL C <560E 85-100 %.
@89>< W6V VAB>B=> =5 2?;820T =0 H284:VABL V ABC?V=L 2A>:BC20==O :0@10<075?V=C.
V2=>206=V :>=F5=B@0FVW ?@5?0@0BC C ?;072V 4>AO30NBLAO G5@57 1-2 B86=V, I> 70;568BL 2V4
V=482V4C0;L=8E >A>1;82>AB59 <5B01>;V7V=4C:FVO D5@<5=B=8E A8AB5< ?5GV=:8 :0@10<075?V=>
<, 35B5@>V=4C:FVO V=H8<8 ;V:0@AL:8<8 70A>10<8, O:V 70AB>A>2CNBL >4=>G0A=>), 0 B0:>6 2V4
AB0=C ?0FVT=B0, 4>78 ?@5?0@0BC V B@820;>ABV ;V:C20==O. !?>AB5@V30NBLAO ACBBT2V
V=482V4C0;L=V 2V4ABV 7=0G5=L @V2=>206=8E :>=F5=B@0FV9 C B5@0?52B8G=>=V: C 1V;LH>ABV
?0FVT=BV2 FV 7=0G5==O :>;820NBLAO 2V4 4 4> 12
V>4>ABC?=VABL @V7=8E ?@5?0@0BV2 :0@10<075?V=C <>65 2V4@V7=OB8AL; B0:0 2;0AB82VABL
40T 7<>3C C=8:=CB8 7W D>@<8, I> <>65 ?@8725AB8 4> 7=865==O 5D5:BC ?@8 70AB>AC20==V :0@10
<075?V=C, ?>O28 5?V;5?B8G=8E =0?04V2 =0 B;V ?@89>3> 70A>1C G8 ?>O28 ?>1VG=8E 5D5:BV2.
>7?>4V: 0 C<>28 ?>2=>W 01A>@1FVW :0@10<075?V=C CO2=89 >1T< @>7?>4V;C AB0=>28BL 2V4 0,8
4> 1,9 ;/:3. 0@10<075?V= ?@>=8:0T :@V7L ?;0F5=B0@=89 10@T@. 2O7C20==O :0@10<075?V=C 7 1V;:0
<8 ?;07<8 :@>2V AB0=>28BL 70-80 %. =>F5=B@0FVO =573> :0@10<075?V=C C A?8==<>7:>2V9
@V48=V V A;8=V ?@>?>@FV9=0 4> G0AB8=8 =572O70=>W 7 1V;:0<8 0:B82=>W @5G>28=8 (20-30 %).
>=F5=B@0FVO :0@10<075?V=C C 3@C4=>2V.
5B01>;V7<. □0@10<075?V= <5B01>;V7CTBLAO C ?5GV=FV ?5@5206=> 5?>:A84=8< H;OE<<,
C=0A;V4>: G>3> CB2>@NNBLAO >A=>2=V <5B01>;VB8 10,11-B@0=A4V>;>25 ?>EV4=5 B0 9>3>
:>=N30B 7 3;N:C@=>2>N :8A;>B>N. A=>2=8< V7>D5@<5=B><, O:89 70157?5GCT 1V>B@0=AD>@
<0FVN :0@10<075?V=C C :0@10<075?V=-10,11-5?>:A84, T F8B>E@< 450 34. #=0A;V4>: F8E
<5B01>;VG=8E @50:FV9 CB2>@NTBLAO B0:>6 V «<0;89» <5B01>;VB 9-3V4@>:A8-<5B8;-10-:0@10
<>W;0:@840=. VA;O >4=>@07>2>3> ?5@>@0;L=>3> 70AB>AC20==O :0@10<075?V=C ?@81;87=> 30 %
0:B82=>W @5G>28=8 287=0G0TBLAO C A5GV C 283;O4V :V=F528E ?@>4C:BV2 5?>:A84=>3>
<5B01>;V7B@0=AD>@<0FVW :0@10<075?V=C A?@8G8=ONBL 4> CB2>@5==O @V7=8E
<>=>3V4@>:A8;0B=8E ?>EV4=8E, 0 B0:>6 N-3;N:C@=>V4C :0@10<075?V=C, I> CB2>@NTBLAO 7
CG0ABN C@848;48D>AD0B-3;N:C@=>78;B@0=AD5@078 (UGT2□7).
82545==O. VA;O >4=>@07>2>3> ?@89> ?5@V>4 =0?V2282545==O =573> :0@10<075?V=C AB0=>28BL
C A5@54=L>48=, 0 ?VA;O ?>2B>@=>3> ?@89>48=8 (2=0A;V4>: 0CB>V=4C:FVW <=>=>:A835=07=>W
A8AB5<8 ?5GV=:8) 70;56=> 2V4 B@820;>ABV ;V:C20==O. # ?0FVT=BV2, O:V >4=>G0A=> ?@89<0NBL
V=HV ?@5?0@0B8, I> V=4C:CNBL BC 6 A0W=, D5=>10@1VB0;), ?5@V>4 =0?V2282545==O :0@10
<075?V=C AB0=>28BL C A5@54=L>48=.
15@54=V9 ?5@V>4 =0?V2282545==O <5B01>;VBC 10,11-5?>:A84C 7 ?;07<8 :@>2V AB0=>28BL
?@81;87=> 6 3>48= ?VA;O @07>2>3> ?5@>@0;L=>3> ?@89>:A84C.
VA;O @07>2>3> ?5@>@0;L=>3> ?@89>W 4>78 282>48BLAO V7 A5G5N C 283;O4V =573> ?@5?0@0BC
V ?@81;87=> 1 % C 283;O4V D0@<0:>;>3VG=> 0:B82=>3> <5B01>;VBC 10,11-5?>:A84C.
A>1;82>ABV D0@<0:>:V=5B8:8 2 >:@5<8E 3@C?0E ?0FVT=BV2.
VB8. VBO< 7>3;O4C =0 1V;LH H284:C 5;V
0FVT=B8 ;VB=L>3> 2V:C. 5<0T 40=8E, O:V A2V4G8;8 1 ?@> B5, I> D0@<0:>:V=5B8:0 :0@10<075?V=C 7
3> 2V:C (?>@V2=O=> 7 4>@>A;8<8 <>;>4>3> 2V:C).
0FVT=B8 7 ?>@CH5=>N DC=:FVTN =8@>: 01> ?5GV=:8. 0=8E ?@> D0@<0:>:V=5B8:C :0@10
<075?V=C C ?0FVT=BV2 7 ?>@CH5==O<8 DC=:FVW =8@>: 01> ?5GV=:8 ?>:8 I> =5<0T.

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

A=>2=V DV78:>-EV 2;0AB82>ABV: B01;5B:8 1V;>3> 01><0965 1V;>3> :>;L>@C, :@C3;>W D>@<8, 7
42>>?C;>N ?>25@E=5N V @8A:>N 7 >4=>3> 1>:C.

"5@ABV. 3 @>:8.

#<>28 715@V30==O.

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

15@V30B8 2 =54>ABC?=>

#?0:>2:0.

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

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

8@>1=8:.

"«!" \$».

VAF57=0E>465==O.

08132, #:@0W=0, 8W2AL:0 >1;., 8T2>-!2OB>H8=AL:89 @-.,