

!" #&/  
4;O <548G=>3> 70AB>AC20==O ?@5?0@0BC

>@VAB0®  
(Lorista®)

!;:04:

4VNG0 @5G>28=0: 1 B01;5B:0, 2:@8B0 ?;V2:>2>N >1>;>=:>N, 12,5 <3 3V4@>E;>@>BV0784C;  
4>?>28=8: :@>E<0;L ?@565;0B8=V7>20=89, F5;N;>70:@8AB0;VG=0, ;0:B>78 <=>3V4@0B, <03=VN  
AB50@0B, 3V?@><5;>70, <0:@>3>; 4000, B0;L.; 10@2=8: EV=>;V=>289 6>2B89 (104), B8B0=C 4V>:A84  
(E 171).

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

\$0@<0:>B5@0?52B8G=0 3@C?0. <>1V=>20=V ?@5?0@0B8 0=B03>=VABV2 0=3V>B5=78=C II.  
>4 " ! !09D 01.

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

>:070==O.

V:C20==O 0@B5@V0;L=>W 3V?5@B5=7VW, :;>8<=>B5@0?VO ;>70@B0=>< 01> <=>B5@0?VO  
3V4@>E;>@>BV0784>< T =54>AB0B=L>N.

@>B8?>:070==O.

V428I5=0 GCB;82VABL 4>;>70@B0=C, @5G>28=, I> T ?>EV4=8<8 AC;LD>=0E;>@>BV0784),  
01> 4> 1C4L-O:8E 4>?> @5G>28=.

03VB=V B0 6V=:8, O:V ?;0=CNBL 70203VB=VB8 (482. @>74V; «0AB>AC20==O C ?5@V>4  
203VB=>ABV 01> 3>4C20==O 3@C44N»).

"06:0 =8@:>20 =54>AB0B=VABL (0 A0<5 ;;V@5=A :@50B8=V=C < 30 <;/E2).

□=C@VO.

8@065=0 ?5GV=:>20 =54>AB0B=VABL, E;>5AB07, >1AB@C:B82=V 70E2>@N20==O  
6>2G>282V4=8E H;OE2.

"5@0?52B8G=> @578AB5=B=0 3V?>:0;VT 3V?5@:0;LF5

!BV9:0 3V?>=0B@VT

!8<0B8G=0 3V?5@C@8:5403@0.

4=>G0A=5 70AB>AC20==O 7 0;VA:V@5=× ?0FVT=B0< 7 FC:@>28< 4V015B<< 01>

?>@CH5==O< DC=:FVW =8@>: ((\$ <60 <;/E2/1,73<2) (482. @>74V;8 «A>1;82>ABV

70AB>AC20==O» B0 «70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9»).

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

>@VAB0® <>6=0 70AB>A>2C20B8 7 V=H8<8 0=B83V?5@B5=782=8<8 70A>10<8.

"01;5B:8 ?@5?0@0BC A;V4 :>2B0B8, 70?820NG8 A;;O=:>N 2>48.

0AB>AC20==O ?@5?0@0BC =5 70;568BL 2V4 ?@89>

@B5@V0;L=0 3V?5@B5=7VO

<>1V=0FVN ;>70@B0=C B0 3V4@>E;>@>BV0784C =5 A;V4 70AB>A>2C20B8 O: ?>G0B:>2C B5@0?VN.  
> <>6;82>ABV 4>FV;L=> B8B@C20B8 4>78 :×=5=BV2 ?@5?0@0BC (>70@B0=C B0  
3V4@>E;>@>BV0784C).

@8 =54>AB0B=V9 5D5:B82=>ABV <=>B5@0?VW :×=5=B0<8 ?@5?0@0BC <>6=0 70AB>A>2C20B8

157?>A5@54=L> :<>1V=>20=89 ?@5?0@0B. 28G09=>N ?>G0B:>2>N B0 ?V4B@8N 4>7>N 4;O

1V;LH>ABV ?0FVT=BV2 T 1 B01;5B:0 ?@5?0@0BC >@VAB0® (50 <3/12,5 <3) 1 @07 =0 4>1C. %2>@8<

C O:8E 70AB>AC20==O 1 B01;5B:8 □>@VAB0® =5 40T 4>AB0B=L>3> 5D5:BC, 4>7C ?@5?0@0BC

<>6=0 ?V428I8B8 4> 2 B01;5B:> □>@VAB0® 1 @07 =0 4>1C (2@0=FV).

0:A8<0;L=89 3V?>B5=782=89 5D5:B 4>AO30TBLAO C <560E 3-4 B86=V2 ;V:C20==O. 0:A8<0;L=> @5:>

<5=4>20=0 4>70 AB0=>28BL 2 B01;5B:8 ?@5?0@0BC □>@VAB0® 1 @07 =0 4>1C.

0AB>AC20==O ?0FVT=B0< V7 =8@:>2>N =54>AB0B=VABN B0 ?0FVT=B0<, O:V ?5@51C20NBL =0 35  
<>4V0;V7V

0FVT=B0< 7 ?>N =8@:>2>N =54>AB0B=VABN (0 A0<5 ;;V@5=A :@50B8=V=C 30-50 <:/E2) :>@5:FVO  
?>G0B:>2>W 4>78 =5 ?>B@V1=0.

>70@B0= B0 3V4@>E;>@>BV0784 C B01;5B:0E =5 @5:><5=4CTBLAO 70AB>A>2C20B8 ?0FVT=B0<,  
O:V ?5@51C20NBL =0 35<>4V0;V7V. >70@B0=/3V4@>E;>@>BV0784 C B01;5B:0E ?@>B8?>:070=89  
?0FVT=B0< V7 BO6:>N =8@:>2>N =54>AB0B=VABN (0 A0<5 ;;V@5=A :@50B8=V=C < 30 <:/E2).

0AB>AC20==O ?0FVT=B0< 7V 7<5=H5==O< 2=CB@VH=L>AC48==>3> >1'TW @V48=8  
>@5:FVN 45DVF8BC >1'T =0B@VN A;V4 ?@>2>48B8 ?5@54 ?>G0B:< 70AB>AC20==O ;>70@B0=C  
/3V4@>E;>@>BV0784C C B01;5B:0E.

0AB>AC20==O ?0FVT=B0< 7 ?5GV=:>2>N =54>AB0B=VABN  
>70@B0=/3V4@>E;>@>BV0784 ?@>B8?>:070=89 ?0FVT=B0< V7 BO6:>N ?5GV=:>2>N  
=54>AB0B=VABN.

0AB>AC20==O ?0FVT=B0< ;VB=L>3> 2V:C  
0FVT=B0< ;VB=L>3> 2V:C :>@83C20==O 4>78, O: ?@028;>, =5 ?>B@V1=5.

>1VG=V @50:FVW.

>1VG=V @50:FVW, O:V <>6CBL 28=8:=CB8 ?V4 G0A ;V:C20==O ;>70@B0=<, ;;0A8DV:>20=V C 3@C?8  
70 G0AB>B>N ?>O28: 4C65 G0AB>: □1/10; G0AB>: □1/100 - <1/10; =5G0AB>: □1/1000 - <1/100; @V4:>:□  
1/10000 - <1/1000; 4C65 @V4:>: <1/10000; =52V4>> (=5 <>6=0 ?V4@0EC20B8 70 =0O2=8<8 40=8<8).  
# 4>A;V465==OE ?@8 0@B5@V0;L=V9 3V?5@B5=7VW 70?0<>@>G5==O 1C;> T48=8< ?>1VG=8<  
5D5:B><, ?>2O70=8< 7 4VNG>N @5G>28=>N V 7CAB@VG02AO ?>=04 1 % E2>@8E (4>AB>2V@=>  
1V;LH =V6 C 3@C?V ?;0F51>).

>@CH5==O 7 I>:C 35?0B>1V;V0@=>W A8AB5<8  
V4:>: 35?0B8B.

@0B>@=8E ?>:07=8:V2  
V4:>: 3V?5@:0;VT

>40B:>2V ?>1VG=V 5D5:B8, O:V A?>AB5@V30;8AO ?@8 70AB>AC20==V >4=>3> 7 >:@5<8E :>=5=BV2  
?@5?0@0BC V <>6CBL 1CB8 ?>B5=V9=8<8 ?>1VG=8<8 5D5:B0<8 ?@5?0@0BC ?@8 70AB>AC20==V  
;>70@B0=C :0;VN/3V4@>E;>@>BV0784C, B0:V:

>70@B0=  
>@CH5==O 7 I>:C A8AB5<8 :@>2V B0 ;VW A8AB5<8  
5G0AB>: 0=5

>@CH5==O 7 I>:C VW A8AB5<8  
V4:>: 0=0DV;0:B8G=V @50:FVW, 0=3V>=52@>B8G=89 =01@O:, :@>?820=:0.

>@CH5==O 7 I>:C <5B01>;V7  
5G0AB>: 0=>@5:AVO, ?>403@0.

A8EVG=V @>7;048  
'0AB>: 157A>==O.

5G0AB>: B@82>30, B@82>6=89 AB0=, A?;CB0=VABL A2V4>>ABV, 45?@5AVO, =VG=V 60EVBBO,  
?>@CH5==O A=C, A>=;82VABL, ?>@CH5==O ?0'OBV.

>@CH5==O 7 I>:C =5@2>2>W A8AB5<8  
'0AB>: 3>;>2=89 1V;L, 70?0<>@>G5==O

5G0AB>: =5@2>7=VABL, ?0@5AB57VW, ?5@8D5@8G=0 =59@>?0BVO, B@5<>@, <=VABL.  
>@CH5==O 7 I>:C >@30=V2 7>@C

5G0AB>: ?>@C, 2V4GCBBO ?5GV==O/A25@1V6 2>G0E, :>='N=:B82VB, ?>@CH5==O 7>@C.  
>@CH5==O 7 I>:C >@30=V2 A;CEC V 25AB81C;O@=>3> 0?0@0BC

5G0AB>: 70?0<>@>G5==O B0 HC< C 2CE0E.  
>@CH5==O 7 I>:C A5@F52>-AC48==>W A8AB5<8

5G0AB>: 0@B5@V0;L=0 3V?>B5=7VO, >@B>AB0B8G=0 3V?>B5=7VO, 1V;L C 3@C4=V9 ;;VBFV,  
AB5=>:0@4VO, 0B@V>25=B@8:C;O@=0 1;>:040 II ABC?5=O, F5@51@>20A:C;O@V ?>@CH5==O,  
V=D0@:B :0@40, 2V4GCBBO A5@F518BBO, 0@8BBV==O ?5@54A5@4L, A8=CA>20 1@048:0@4VO,  
B0EV:0@4VO, H;C=>G:>20 B0EV:0@4VO, DV1@8;OFVO H;C=>G:V2 A5@FO).

>@CH5==O 7 I>:C AC48==>W A8AB5<8  
5G0AB>: 20A:C;VB.

>@CH5==O 7 I>:C 48E0;L=>W A8AB5<8 B0 >@30=V2 A5@54>ABV==O  
'0AB>: :0H5;L, 70?0;5==O 25@E=VE 48E0;L=8E H;OEV2, 70::045=VABL =>A0, 309<>@8B, 7A>28E  
?07CE0E.  
5G0AB>: 2V4GCBBO D0@8=350;L=>3> 48A:>@BC, D0@8=3VB, ;0@8=3VB, 7048H:0, 1@>=EVB,  
=>A>20 :@>2>B5G0, @8=VB, ?>@CH5==O ?@>EV4=>ABV 48E0;L=8E H;OEV2.  
>@CH5==O 7 I>:C B@02=>3> B@0:BC  
'0AB>: 1V;L C 682>BV, =C4>B0, 4V0@50, 48A?5?AVO.  
5G0AB>: 70?>@, 7C1=89 1V;L, ACEVABL C @>BV,<5B5>@87<, 30AB@8B, 1;N20==O.  
>@CH5==O 7 I>:C 35?0B>1V;V0@=>W A8AB5<8  
52V4><: DC=:FV>=0;L=V ?>@CH5==O ?5GV=:8.  
>@CH5==O 7 I>:C H:V@8 V?V4H:V@=8E B:0=8=  
=>4V: 0;>?5FVO, 45@<0B8B, ACEVABL H:V@8, 5@8B5<0, ?>G5@2>=V==O, A2VB;>GCB;82VABL,  
A25@1V6, 28A8?0==O, :@>?82'O=:0, ?V428I5=5 ?>B>284V;5==O.  
>@CH5==O 7 I>:C :VAB:>2>-<O7>2>W A8AB5<8 B0 A?>;CG=8E B:0=8=  
'0AB>: <'O7>2V AC4<8, 1V;L C A?8=V, 1V;L C =>30E,  
5G0AB>: 1V;L C @C:0E, =01@O:8 AC3;>1V2, 1V;L C :>;V=0E, :VAB:>2V V<'O7>2V 1>;V, 1V;L C ?;5G0E,  
2V4GCBBO A:CB>ABV C AC3;>10E, 0@B@0;3VO, 0@B@8B, :>:A0;3VO, DV1@>1V.  
C65 @V4>: @014>;V7.  
>@CH5==O 7 I>:C =8@>: B0 A5G>282V4=8E H;OEV2  
5G0AB>: =V:BC@VO, V=B5=A82=5 284V;5==O A5GV, V=D5:FVW A5G>282V4=8E H;OEV2.  
>@CH5==O 7 I>:C @5?@>4C:B82=>W A8AB5<8 B0 <>;>G=8E 70;>7  
5G0AB>: 7=865==O ;V1V4>, VB5=FVO.  
!8AB5<=V ?>@CH5==O B0 CA:;04=5==O C  
'0AB>: ?V428I5=0 2B<;N20==VABL, 1V;L C 3@C4=V9 ;;VBFV.  
5G0AB>: =01@O: >1;8GGO, ?V428I5==O B5  
@0B>@=8E ?>:07=8:V2  
'0AB>: 3V?5@:0;VT  
5G0AB>: =57=0G=5 7=865==O :>=F5=B@0FVW 70;8H:>2>3> 07>BC B0 :@50B8=V=C.  
C65 @V4>: 71V;LH5==O 0:B82=>ABV ?5GV=:>28E D5@<5=BV2 V @V2=O 1V;V@C1V=C.  
V4@>E:>@>BV0784  
>@CH5==O 7 I>:C A8AB5<8 :@>2V B0 ;VW A8AB5<8  
5G0AB>: 03@0=C;>F8B>7, 0?;0AB8G=0 0=5?5=VO, ?C@?C@0, B@><1>F8B>?5=VO.  
>@CH5==O 7 I>:C VW A8AB5<8  
V4>: 0=0DV;0:B8G=0 @50:FVO.  
>@CH5==O 7 I>:C <5B01>;V7  
5G0AB>: 0=>@5:AVO, 3V?5@3;V:50;VT=0B@VT  
A8EVG=V @>7;048  
5G0AB>: 157A>==O, 7N.  
>@CH5==O 7 I>:C =5@2>2>W A8AB5<8  
'0AB>: 3>;>2=89 1V;L.  
>@CH5==O 7 I>:C >@30=V2 7>@C  
5G0AB>: B825 ?>@C, :A0=B>?AVO.  
>@CH5==O 7 I>:C AC48==>W A8AB5<8  
5G0AB>: =5:@>B87CNG89 0=3VWB (20A:C;VB V H:V@=89 20A:C;VB).  
>@CH5==O 7 I>:C 48E0;L=>W A8AB5<8 B0 >@30=V2 A5@54>ABV==O  
5G0AB>: @5A?V@0B>@=89 48AB@5A, 2;;NG0NG8 ?=52<>=VB B0 =01@O: ;535=V2.  
>@CH5==O 7 I>:C B@02=>3> B@0:BC  
5G0AB>: 70?0;5==O A;8==8E 70;>7, :8H:>2V A?07<8, ?>4@07=5==O H;C=:0, =C4>B0, 1;N20==O,  
4V0@50, 70?>@8.  
>@CH5==O 7 I>:C 35?0B>1V;V0@=>W A8AB5<8  
5G0AB>: 6>2BO=8FO (2=CB@VH=L>?5GV=:>20 E>;5AB0B8G=0), ?0=:@50B8B.  
>@CH5==O 7 I>:C H:V@8 V?V4H:V@=8E B:0=8=  
5G0AB>: A2VB;>GCB;82VABL, :@>?82'O=:0, B>:A8G=89 5?V45@<0;L=89 =5:@>;V7.  
5G0AB>: A8=4@>< !BV25=A0-6>=A>=0; H:V@=V @50:FVW, I> =0304CNBL H:V@=C D>@  
>@CH5==O 7 I>:C :VAB:>2>-<O7>2>W A8AB5<8 B0 A?>;CG=8E B:0=8=

5G0AB>: <'O7>2V AC4<8.

>@CH5==O 7 I>:C =8@>: B0 A5G>282V4=8E H;OEV2

5G0AB>: 3;N:>7C@VO, V=B5@AB8FV0;L=89 =5D@8B, 48ADC=:FVO =8@>:, =8@>:20 =54>AB0B=VABL.

!8AB5<=V ?>@CH5==O B0 CA.;04=5==O C

5G0AB>: ?V428I5==O B5@>G5==O.

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

!75F8DVG=8E 40=8E I>4> ;V:C20==O ?5@54>7C20==O ?@5?0@0B< =5<0T. "5@0?VO ?5@54>7C20==O A8<0B8G=0 V ?V4B@8B@V1=> ?5@5@20B8 :C@A B5@0?VW ?@5?0@0B< V @5B5;L=>

:>=B@>;N20B8 AB0= ?0FVT=B0. /:I> ?@5?0@0B ?@89=OB> =5I>402=>, ?>B@V1=> 28;;8:0B8 1;N20==O V 70AB>AC20B8 70E>48, A?@O<>20=V =0 CAC=5==O 453V4@0B0FVW, 5;5:B@>;VB=8E ?>@CH5=L, ?5GV=:>2>W :<8 B0 0@B5@V0;L=>W 3V?>B5=7VW.

>70@B0=

0=V ?@> ?5@54>7C20==O ?@5?0@0BC C ;N459 >1<565=V. 091V;LH V<>2V@=8<8 ?@>O20<8

?5@54>7C20==O T 0@B5@V0;L=0 3V?>B5=7V0, B0EV:0@4V0; 1@048:0@4V0<>65 1CB8 =0A;V4:<< ?0@0A8W (203CA=>W) AB8

>70@B0= V 9>3> 0:B82=89 <5B01>;VB =5 2840;ONBLAO H;OE<< 35<>4V0;V7C.

V4@>E;>@>BV0784

09G0ABVHV A8<8 ?5@54>7C20==O T =0A;V4:< 45DVF8BC 5;5:B@>;VBV2 (3V?>:0;VTE;>@5=0B@VT : =043> A5G>284V;5==O. @8 >4=>G0A=>784V2 3V?>:0;VT

V4@>E;>@>BV0784 2840;OTBLAO H;OE<< 35<>4V0;V7C, ?@>B5 ABC?V=L 2840;5==O =5 1C2 2AB0=>2;5=89.

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

03VB=VABL

V:0@AL:89 70AV1 ?@>B8?>:070=> 70AB>A>2C20B8 203VB=8< 01> 6V=:0<, O:V ?;0=CNBL

70203VB=VB8. /:I> ?V4 G0A ;V:C20==O ?@5?0@0B< ?V4B25@46CTBLAO 203VB=VABL, 9>3>

70AB>AC20==O =5>1EV4=> =5309=> ?@8?8=8B8 V 70□V4<>, I> 70AB>AC20==O V=3V1VB>@V2

0=3V>B5=78=C ?V4 G0A 9 B@8<5AB@C 203VB=>ABV <>65 A?@8G8=OB8 D5B>B>:A8G=VABL

(7=865==O DC=:FVW =8@>:, >;V3>3V4@0<=V>= 7 3V?>?;07VTN ;535=L, @5B0@40FVN >:>AB5=V==O G5@5?0) V =5>=0B0;L=C B>:A8G=VABL (=8@>:2C =54>AB0B=VABL, 0@B5@V0;L=C 3V?>B5=7VN, 3V?5@:0;VT

/:I> 70AB>AC20==O V=3V1VB>@V2 0=3V>B5=78=C 2V41C;>AO 2 B@8<5AB@V 203VB=>ABV, @5:> <5=4CTBLAO ?@>25AB8 C;LB@072C:>25 4>A;V465==O DC=:FVW =8@>: B0 G5@5?0.

5<>2;OB, <0B5@V O:8E ?@89<0;8 V=3V1VB>@8 0=3V>B5=78=C , A;V4 @5B5;L=> :>=B@>;N20B8 =0 ?@54<5B 0@B5@V0;L=>W 3V?>B5=7VW, >;V3C@VW B0 3V?5@:0;VT74V; «@>B8?>:070==O», «A>1;82>ABV 70AB>AC20==O»).

V4@>E;>@>BV0784

A=CT >1<565=89 4>A2V4 70AB>AC20==O 3V4@>E;>@>BV0784C ?V4 G0A 203VB=>ABV, >A>1;82> ?V4 G0A

B@8<5AB@C. >A;V465==O =0 B20@8=0E >1<565=V.

V4@>E;>@>BV0784 ?@>=8:0T G5@57 ?;0F5=B0@=89 10@T@. 0 >A=>2V D0@<0>;>3VG=>3> <5E0=V7 E;>@>BV0784C, 9>3> 70AB>AC20==O ?V4 G0A B0 B@8<5AB@C <>65 70H:>48B8 :@>2?>AB0G0==N

N B0 ?;>4>< V A?@8G8=8B8 C ?;>40 B0 =5<>2;OB8 6>2BO=8FN, @>7;04 5;5:B@>;VB=>3> 10;0=AC B0 B@><1>F8B>?5=VN.

V4@>E;>@>BV0784 =5 A;V4 70AB>A>2C20B8 4;O ;V:C20==O 35AB0FV9=>3> =01@O:C, 0 B0:>6 35AB0FV9=>W 0@B5@V0;L=>W 3V?5@B5=7VW 01> ?@55::01□T

V4@>E;>@>BV0784 =5 A;V4 70AB>A>2C20B8 4;O ;V:C20==O 0@B5@V0;L=>W 3V?5@B5=7VW C 203VB=8E 6V=>:, 70 28=OB:>< 28?04:V2, :>;8 =5 <>6=0 70AB>A>2C20B8 0;LB5@=0B82=5 ;V:C20==O.

>4C20==O 3@C44N

5 @5:><5=4CTBLAO 70AB>A>2C20B8 ?@5?0@0B, G5@57 2V4ACB=VABL 4>AB0B=VE 40=8E I>4>

70AB>AC20==O C ?5@V>4 3>4C20==O 3@C44N. 0FVT=B0 A;V4 ?5@525AB8 =0 0;LB5@=0B82=5

0=B83V?5@B5=782=5 ;V:C20==O, O:5 <0T 70B25@465=89 ?@>DV;L 157?5:8 70AB>AC20==O C ?5@V>4 3>4C20==O 3@C44N, >A>1;82> =>2>=0@>465=8E 01> =54>=>H5=8E 4VB59.

**VB8.**

>A2V4 70AB>AC20==O ?@5?0@0BC 4;O ;V:C20==O 4VB59 2V4ACB=V9, B>70@B0=/  
3V4@>E;>@>BV0784 =5 A;V4 70AB>A>2C20B8 40=V9 :0B53>@VW ?0FVT=V2.

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

>70@B0=

V428I5=0 GCB;82VABL

>6;825 28=8:=5==O 0=3V>=52@>B8G=>3> =01@O:C. !;V4 2AB0=>28B8 @5B5;L=89 :>=B@>;L 70  
?0FVT=B0<8, 2 O:8E 2 0=0<=57V 1C2 0=3V>=52@>B8G=89 =01@O: (=01@O: >1;8GGO, 3C1, 3>@B0=V  
B0/01> O78:0).

@B5@V0;L=0 3V?>B5=7VO B0 ?>@CH5==O 2>4=>-5;5:B@>;VB=>3> 10;0=AC

# ?0FVT=V2 V7 45DVF8B><>1T F8@:C;NT, B0/01> =0B@VN 2 >@30=V7: V=B5=A82=>3>

70AB>AC20==O 4VC@5B8:V2, >1<565==O 26820==O A>;V, 4V0@5W 01> 1;N20==O,<>65 28=8:0B8 A8  
<0B8G=0 0@B5@V0;L=0 3V?>B5=7VO, >A>1;82> ?VA;O ?@89>W 4>78 B0 ?VA;O ?V428I5==O 4>78.

>4V1=V AB0=8 28<030NBL ?@>2545==O WE :>@5:FVW 4> 70AB>AC20==O ?@5?0@0BC 01> 7

<5=H5==O ?>G0B:>2>W 4>78.

>@CH5==O 2>4=>-5;5:B@>;VB=>3> 10;0=AC

# ?0FVT=V2 V7 =8@:>2>N =54>AB0B=VABN, O: E2>@8E =0 FC:@>289 4V015B, B0: V 157 =L>3>,  
G0AB> 28=8:0NBL ?>@CH5==O 5;5:B@>;VB=>3> 10;0=AC, O:V 28<030NBL :>@5:FVW. V4 G0A

::V=VG=8E 28?>@1C20=L, ?@>2545=8E A5@54 ?0FVT=V2 7 4V015B>< II B8?C B0 =5D@>?0BVTN,  
G0AB>B0 28=8:=5==O 3V?5@:0;VTN C 3@C?V, O:0 >B@870@B0=, ?>@V2=O=> 7 3@C?>N ?;0F51>. ">  
1EV4=> @53C;O@=> :>=B@>;N20B8 :>=F5=B@0FVN :0;VN C ?;072V B0 ?>:07=8:8 ;;V@5=AC

:@50B8=V=C. A>1;82> @5B5;L=>3> A?>AB5@565==O 28<030NBL ?0FVT=B8 7 A5@F52>N

=54>AB0B=VABN B0 ;;V@5=A< :@50B8=V=C 2V4 30 4> 50 <;E2 4=>G0A=> 7 ;>70@B0=>< =5 @5:>

<5=4CTBLAO 70AB>A>2C20B8 :0;V9715@V30NGV 4VC@5B8:8, 4>102:8, I> ;V 7 :0;VT

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

h@C=BCNG8AL =0 D0@<0>:V=5B8G=8E 40=8E, O:V A2V4G0BL ?@> ACBBT25 71V;LH5==O

:>=F5=B@0FV9 ;>70@B0=C C ?;072V C ?0FVT=V2 V7 F8@>7< ?5GV=:8, ?0FVT=B0<, 2 0=0<=57V C

O:8E T ?>@CH5==O DC=:FVW ?5GV=:8, =5>1EV4=> 7<5=H8B8 4>7C ?@5?0@0BC. >A2V4C

B5@0?52B8G=>3> 70AB>AC20==O ;>70@B0=C ?0FVT=B0< V7 BO6:>N ?5GV=:>2>N =54>AB0B=VABN

=5<0T. ">70@B0= =5 <>6=0 ?@89<0B8 ?0FVT=B0< V7 BO6:>N ?5GV=:>2>N =54>AB0B=VABN.

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

/: =0A;V4>: V=3V1C20==O @5=V=-0=3V>B5=78=>2>W A8AB5<8, A?>AB5@V30;8AO 7=C20==V =8@>;

C B>20 =54>AB0B=VABL (7>:@5<0 C ?0FVT=V2, C O:8E @>1>B0 =8@>: 70;568BL 2V4

DC=:FV>=C20==O @5=V=-0=3V>B5=78=-0;L4>AB5@>=>2>W A8AB5<8, =0?@8;:04 ?@8 BO6:V9

A5@F52V9 =54>AB0B=>ABV 01> =0O2=>ABV D>=>2>W 48ADC=:FVW =8@>:). /: V ?@8

70AB>AC20==V V=H8E ?@5?0@0BV2, I> 2?;820NBL =0 @5=V=-0=3V>B5=78=-0;L4>AB5@>=>2C

A8AB5AB>@>=V< AB5=>7< =8@:>2>W 0@B5@VW 01> AB5=>7< =8@:>2>W 0@B5@VW T48=>W

=8@:8 A?>AB5@V30TBLAO 71V;LH5==O @V2=O A5G>28=8 :@>2V B0 A8@>20B:>2>3> :@50B8=V=C.

>70@B0= A;V4 7 >15@56=VABN 70AB>A>2C20B8 ?0FVT=B0< V7 42>AB>@>=V< AB5=>7<

=8@:>28E 0@B5@V9 01> AB5=>7< =8@:>2>W 0@B5@VW T48=>W =8@:8.

"@0=A?;0=B0FVO =8@:8

>A2V4C 70AB>AC20==O ?@5?0@0BC ?0FVT=B0<, O:V =5I>402=> ?5@5=5A;8 B@0=A?;0=B0FVN

=8@>;, =5<0T.

5@28==89 3V?5@0;L4>AB5@>=V7<

0FVT=B8 7 ?5@28==8< 0;L4>AB5@>=V7<<<, O: ?@028;>, =5 @503CNBL =0 ;V:C20==O

0=B83V?5@B5=782=8<8 ?@5?0@0B0<8, <5E0=V7< 4VW O:8E ?>;O30T C ?@83=VG5==V @5=V=-

0=3V>B5=78=>2>W A8AB5<8. ">.

H5@>10 A5@FO B0 F5@51@>20A:C;O@=5 70E2>@N20==O

/: V ?@8 70AB>AC20==V 1C4L-O:8E V=H8E 0=B83V?5@B5=782=8E ?@5?0@0BV2, H284:5 7=865==O

0@B5@V0;L=>3> B8A:C C ?0FVT=V2 7 VH5N E2>@>1>N A5@FO B0 F5@51@>20A:C;O@=8<

70E2>@N20==O< <>65 A?@8G8=8B8 V=D0@:B :0@40 01> V=AC;LB.

!5@F520 =54>AB0B=VABL

# ?0FVT=V2 V7 A5@F52>N =54>AB0B=VABN, 7 ?>@CH5==O< DC=:FVW =8@>: G8 157, ?@8

70AB>AC20==V ;>70@B0=C, O:V V ?@8 70AB>AC20==V 1C4L-O:8E V=H8E ;V:0@AL:8E 70A>1V2, I->4VNBL =0 @5=V=-0=3V>B5=78=>2C A8AB5W 0@B5@V0;L=>W 3V?>B5=7VW B0 (4C65 G0AB>3>AB@>W) =8@:>2>W =54>AB0B=>ABV. # ?0FVT=BV2 V7 A5@F52>N =54>AB0B=VABN B0 AC?CB=L>N BO6:>N =8@:>2>N =54>AB0B=VABN, C ?0FVT=BV2 V7 BO6:>N =8@:>2>N =54>AB0B=VABN (IV ;:0A 70 ;:0A8DV:0FVTN NYHA), 0 B0:>6 C ?0FVT=BV2 V7 A5@F52>N =54>AB0B=VABN B0 A5@F528<8 0@8B.

!B5=>7 0>@B0;L=>3> B0 3> ;:0?0=0, >1AB@C:B82=0 3V?5@B@>DVG=0 :0@4V>?0BV0 /: V ?@8 70AB>AC20==V V=H8E 207>48;0B0B>@V2, A;V4 28O2;OB8 >A>1;82C >15@56=VABL C ?0FVT=BV2 7V AB5=>7< 0>@B0;L=>3> 01> 3> ;:0?0=0 01> >1AB@C:B82=>N 3V?5@B@>DVG=>N :0@4V>?0BV0TN.

03VB=VABL

@89>< 0=B03>=VABV2 @5F5?B>@V2 0=3V>B5=78=C =5 A;V4 @>7?>G8=0B8 C ?5@V>4 203VB=>ABV. /:I> ?@>4>265==O B5@0?VW 0=B03>=VAB0<8 @5F5?B>@V2 0=3V>B5=78=C =5 22060TBLAO 206;828<, ?0FVT=B>:, O:V ?;0=CNBL 203VB=VABL, A;V4 ?5@525AB8 =0 0;LB5@=0B82=5 0=B83V?5@B5=782=5 ;V:C20==O, O:5 <0T 70B25@465=89 ?@>DV;L 157?5:8 70AB>AC20==O ?V4 G0A 203VB=>ABV. /:I> 28O2;5=0 203VB=VABL, ;V:C20==O ;>70@B0=× A;V4 =5309=> ?@8?8=8B8, B0, O:I> F5 <>6;82>, A;V4 @>7?>G0B8 0;LB5@=0B82=C B5@0?VN.

=HV ?>?5@5465==O V 70AB5@565==O

>4V1=> 4> V=3V1VB>@V2 0=3V>B5=78=?5@5B2>@N20;L=>3> D5@<5=BC, ;>70@B0= B0 V=HV 0=B03>=VAB8 0=3V>B5=78=C T<5=H 5D5:B82=8<8 C 7=865==V 0@B5@V0;L=>3> B8A:C C G>@=>H:V@8E ?0FVT=BV2, ?>@V2=O=> 7 ?@54AB02=8:0<8 V=H8E @0A, =09V<>2V@=VH5, 2=0A;V4>: 1V;LH 28A>:>W G0AB>B8 >AV1 V7 =87L:8< @V2=5< @5=V=C C ?>?C;OFVW G>@=>H:V@8E ?0FVT=BV2 70 0@B5@V0;L=>N 3V?5@B5=7VTN.

>42V9=0 1;>:040 @5=V=-0=3V>B5=78=-0;L4>AB5@>=>2> W A8AB5<8 (!)

@8 AC?CB=L>AC20==V 0;VA:V@5=C B0 0=B03>=VABV2 @5F5?B>@V2 0=3V>B5=78=C 01> V=3V1VB>@V2 \$ ?V428ICTBLAO @878: 0@B5@V0;L=>W 3V?>B5=7VW, 3V?5@:0;VT:, 2;;NG0NG8 3>AB@C =8@:>2C =54>AB0B=VABL. # 72O7:C 7 ?>42V9=>N 1;>:04>N @5=V=-0=3V>B5=78=-0;L4>AB5@>=>2>W A8AB5<8 (!) AC?CB=T 70AB>AC20==O 0;VA:V@5=C B0 0=B03>=VABV2 @5F5?B>@V2 0=3V>B5=78=C 01> V=3V1VB>@V2 \$ =5 @5:>5=4CTBLAO (482.@>74V; «□70T<>4V0 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9»). # 28?04:C :@09=L>W =5>1EV4=>ABV ?>42V9=>W 1;>:048 ! A;V4 @5B5;L=> ?5@52V@OB8 DC=:FVN =8@>:, @V25=L 5;5:B@>;VBV2 C :@>2V B0 0@B5@V0;L=89 B8A:. 5 A;V4 >4=>G0A=> 70AB>AC20B8 0=B03>=VAB8 @5F5?B>@V2 0=3V>B5=78=C B0 V=3V1VB>@8 \$ ?0FVT=B0< 7 FC:@>28< 4V015B>

V4@>E;>@>BV0784

@B5@V0;L=0 3V?>B5=7V0 B0 ?>@CH5==O 2>4=>-5;5:B@>;VB=>3> 10;0=AC

/: V ?@8 70AB>AC20==V V=H8E 70A>1V2 0=B83V?5@B5=782=>W B5@0?VW, C 45O:8E ?0FVT=BV2 <>6;8289 @>728B>: A8<0B8G=>W 3V?>B5=7VW. 0FVT=B8 ?>28==V 1CB8 >1AB565=V 7<5B>N 28O2;5==O ;V=VG=8E >7=0: ?>@CH5==O 2>4=>-5;5:B@>;VB=>3> 10;0=AC, =0?@8::04 =5AB0GV @V48=8, 3V?>=0B@VTE;>@53> 0;:0;>7C, 3V?><03=VT 3V?>:0;VT2>48B8 ?5@V>48G=5 287=0G5==O A8@>20B:>28E 5;5:B@>;VBV2. 8;NFV9=0 3V?>=0B@VT

5B01>;VG=V B0 5=4>:@8==V 5D5:B8

"V07848 740B=V 7;5@0=B=VABL 4> 3;N:>78. >65 1CB8 ?>B@V1=>N :>@5:FVO 4>7 0=B84V015B8G=8E ?@5?0@0BV2, 2;;NG0NG8 V=AC;V=. V4 G0A B5@0?VW BV07840<8 ?@8E>20=89 FC:@>289 4V015B <>65 ?@>O28B8AO.

"V07848 <>6CBL 7<5=HC20B8 5:A:@5FVN :0;LFVN 7 A5G5N. "V07848 <>6CBL B0:>6 28::8:0B8 =57=0G=5 V A:>@>8=CI5 7@>AB0==O @V2=O :0;LFVN C A8@>20BFV :@>2V. 8@065=0 3V?5@:0;LFVT

V428I5==O @V2=V2 E>;5AB5@8=C V B@83;VF5@84V2 B0:>6 <>65 1CB8 ?>2'O70=5 7 B5@0?VTN 4VC@5B8:0<8 BV0784>2>3> @O4C.

"5@0?VO BV07840<8 <>65 ?@8725AB8 4> 3V?5@C@V:5 ?>403@8 C 45O:8E ?0FVT=BV2. '5@57 B5, I> ;>70@B0= 7<5=HCT 22>W :8A;>B8, ;>70@B0= C :><1V=0FVW 7 3V4@>E;>@>BV0784< 7<5=HCT 3V?5@C@8:5

5GV=:>20 =54>AB0B=VABL

"V07848 A;V4 70AB>A>2C20B8 7 >15@56=VABN ?0FVT=B0< 7 ?>@CH5==O< DC=:FVW ?5GV=:8 01> ?@>3@5ACNG>N E2>@>1>N ?5GV=:8, >A;V;L:8 2V= <>65 A?@8G8=8B8 ?>O2C 2=CB@VH=L>?5GV=:>2>3> E>;5AB07C B0 >A;V;L:8 =57=0G=V 74=>-5;5:B@>;VB=>3> 10;0=AC <>6CBL A?@8G8=8B8 ?5GV=:>2C :>B8?>:070=89 ?0FVT=B0< V7 BO6:>N ?5GV=:>2>N =54>AB0B=VABN.

=HV AB0=8

# ?0FVT=BV2, O:V >B@8

A>I;820 V=D>@<0FVO ?@> 45O:V 7 4>?>28=

@5?0@0B 7C. 0FVT=B0< V7 @V4:VA=8<8 A?04:>28<8 D>@<0<8 =5?5@5=>A8<>ABV 30;0:B>78, 45DVF8B>< ;0:B078 01> ?>@CH5==O< 2A<>:BC20==O 3;N:>78-30;0:B>78 =5 A;V4 ?@89<0B8 F59 ?@5?0@0B.

**40B=VABL 2?;820B8 =0 H284:VABL @50:FVW ?@8 :5@C20==V 02B>B@0=A?>@B< 01> @>I>BV 7 V=H8<8 <5E0=V7<0<8.**

>3;04C =0 <>6;82VABL @>728B:C B0:8E ?>1VG=8E @50:FV9 O: 70?0<>@>G5==O B0 0@B5@V0;L=0 3V?>B5=7VO, ?@5?0@0B A;V4 70AB>A>2C20B8 7 >15@56=VABN ?@8 :5@C20==V 02B>B@0=A?>@B< 01> @>I>BV 7 V=H8<8 <5E0=V7<0<8.

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

>70@B0=

C;8 ?>2V4><;5==O ?@> B5, I> @8D0=07>; 7=86CNBL @V25=L 0:B82=>3> <5B01>;VBC. ;V=VG=V =0A;V4:8 F8E 270T<>4V9 =5 >FV=N20;8AO.

/: V V=HV ?@5?0@0B8, I> 1;>:CNBL @5F5?B>@8 0=3V>B5=78=C II 01> WE 5D5:B8, AC?CB=V9 ?@89> < :0;V9715@V30NG8E 4VC@5B8:V2 (=0?@8;:04, A?V@=>=>0:B>=C, B@V0@84C), :0;VT28E 4>102>: 01> A>;L>28E 70

/: V ?@8 70AB>AC20==V V=H8E ;V:0@AL:8E 70A>1V2, O:V 2?;820NBL =0 282545==O =0B@VN, <>65 1CB8 7<5=H5=5 282545==O ;VBN. "> :>=B@>;N20B8 @V25=L ;VBN 2 A8@>20BFV, O:I> A>;V ;VBN 70AB>A>2CNBL @07< 7 0=B03>=VAB0<8 @5F5?B>@V2 0=3V>B5=78=C II.

5AB5@>W4=V ?@>B870?0;L=V ;V:0@AL:V 70A>18 (0F5B8;A0;VF8;>20 :8A;>B0 2 @568B870?0;L=>3> 4>7C20==O, A5;5:B82=V V=3V1VB>@8 &-2) B0 =5A5;5:B82=V =5AB5@>W4=V ?@>B870?0;L=V ;V:0@AL:V 70A>18 <>6CBL 7<5=H8B8 0=B83V?5@B5=782=89 5D5:B 0=B03>=VABV2 @5F5?B>@V2 0=3V>B5=78=C II. !C?CB=V9 ?@89>< 0=B03>=VABV2 @5F5?B>@V2 0=3V>B5=78=C II 01>

4VC@5B8:V2 B0 =5AB5@>W4=8E ?@>B870?0;L=8E ;V:0@AL:8E 70A>1V2 <>65 ?@8725AB8 4> ?>3V@H5==O DC=:FVW =8@>:, 2;;NG0NG8 <>6;82C 3>AB@C =8@>:2C =54>AB0B=VABL, B0 71V;LH5==O @V2=O :0;VN 2 A8@>20BFV, >A>1;82> C ?0FVT=BV2 7 ?>@CH5==O< DC=:FVW =8@>:.

"0:C :<1V=0FVN A;V4 ?@89<0B8 7 >15@56=VABN, >A>1;82> >A>10< ;VB=L>3> 2V:C. 0FVT=B8 ?>B@51CNBL 70157?5G5==O 045:20B=>W 3V4@0B0FVW V ?@>2545==O @5B5;L=>3> :>=B@>;N DC=:FVW =8@>: =0 ?>G0B:C AC?CB=L>W B5@0?VW B0 ?5@V>48G=> ?VA;O =5W.

# 450:8E ?0FVT=BV2 7 ?>@CH5==O< DC=:FVW =8@>: AC?CB=V9 ?@89>< 0=B03>=VABV2 @5F5?B>@V2 0=3V>B5=78=C II B0 ?@5?0@0BV2, O:V ?@83=VGCNBL F8;:>>:A835=07C 2, <>65 ?@8725AB8 4> ?>40;LH>3> ?>3V@H5==O DC=:FVW =8@>: &V 5D5:B8, O: ?@028;>, T >1>@>B=8<8. =HV ?@5?0@0B8, O:V <>6CBL A?@8G8=8B8 0@B5@V0;L=C 3V?>B5=7VN O: >A=>2=5

70E2>@N20==O 01> ?>1VG=89 5D5:B, F5 B@8F8;VG=V 0=B845?@5A0=B8, =59@>;5?B8:8, 10;:>D5=, 0 AB8=. !C?CB=T 70AB>AC20==O F8E ?@5?0@0BV2 <>65 ?V428I8B8 @878: 0@B5@V0;L=>W 3V?>B5=7VW.

>A;V465==O ?>:070;8, I> 2=0A;V4>: ?>42V9=>W 1;>:048 ! ?@8 AC?CB=L>AC20==V V=3V1VB>@V2 \$, 0=B03>=VABV2 @5F5?B>@V2 0=3V>B5=78=C 01> 0;VA:V@5=C ?V428ICTBLAO @878: ?>1VG=8E @50:FV9 B0:8E O:, 0@B5@V0;L=0 3V?>B5=7VO, 3V?5@:0;VT:, 2;;NG0NG8 3>AB@C =8@>:2C =54>AB0B=VABL ?>@V2=O=> V7 70AB>AC20==O< >4=>3> 035=B0 @5=V=-0=3V>B5=78=-

0;L4>AB5@>=>2>W A8AB5<8 (482. @>74V;8 «@>B8?>:070==O», «A>1;82>ABV 70AB>AC20==O».

V4@>E:>@>BV0784

@8 >4=>G0A=>AC20==V 707=0G5=V ?@5?0@0B8 <>6CBL 270T<>4VOB8 7 4VC@5B8:0<8

BV0784>2>3> @O4C:

;:>3>;L, 10@IVBC@0B8, =0@:>B8G=V 70A>18 01> 0=B845?@5A0=B8

>65 ?>A8;8B8AO >@B>AB0B8G=0 3V?>B5=7VO.

=B84V015B8G=V 70A>18 (?5@>@0;L=V ?@5?0@0B8 B0 V=AC;V=)  
0AB>AC20==O BV0784V2 <>65 2?;820B8 =0 ?5@5=>A878. >65 28=8:=CB8 =5>1EV4=VABL C 778  
0=B84V015B8G=8E 70A>1V2. 5BD>@A>2C20B8 7 >15@56=VABN, >A;V;L:8 VA=CT @878: 28=8:=5==O  
;0:B>F84>7C, A?@8G8=5=>3> <>6;82>N DC=:FV>=0;L=>N =54>AB0B=VABN =8@>;, ?>2O70=>3> 7  
70AB>AC20==O< 3V4@>E;>@>BV0784C.  
=HV 3V?>B5=782=V 70A>18  
48B82=89 5D5:B.  
%>;5AB8@0;5AB8?>;, A<>;8  
# ?@8ACB=>ABV 0=V=>=>1;5AB8?>;C 72'O7CT 3V4@>E;>@>BV0784 V 2V4?>2V4=> =0 85 % 01> =0  
43 % 7=86CT 9>3> 2A<:BC20==O 7 H;C=:>2>:8H:>2>3> B@0:BC.  
>@B8:>AB5@>W48, "  
1V;LHCTBLAO 2B@0B0 5;5:B@>;V BV2, >A>1;82> @878: 28=8:=5==O 3V?>:0;VT  
@5A>@=V 0  
>6;825 7=865==O @50:FVW =0 ?@5A>@=V 03> 7=865==O =57=0G=0, B>AC20==O F8E 70A>1V2.  
545?>;O@87CNGV A:5;5B=>-<'O7>2V @5;0:A0=B8 (=0?@8:;04 BCI>:C@0@8=)  
>6;825 ?>A8;5==O 2V4?>2V4V =0 <'O7>2V @5;0:A0=B8.  
@5?0@0B8 ;VBVN  
VC@5B8:8 7<5=HCNBL ;V@5=A ;VBVN 2 =8@:0E V ?V428ICNBL @878: ;VBVT2>W V=B>:A8:0FVW;  
AC?CB=T 70AB>AC20==O =5 @5:>5=4CTBLAO.  
@5?0@0B8, O:V 70AB>A>2CNBLAO 4;O ;V:C20==O ?>403@8 (?@>15=5F84, AC;LDV=?V@07>= V  
0;>?C@8=>;)  
>65 AB0B8 =5>1EV4=8< 778 ?@5?0@0BV2, I> 282>4OBL A5G>2C :8A;>BC, B>3V4@>E;>@>BV0784  
<>65 71V;LHC20B8 :=F5=B@0FVN A5G>2>W :8A;>B8 C ?;072V. >65 AB0B8 =5>1EV4=8< 71V;LH5==O  
4>78 ?@>15=5F84C 01> AC;LDV=?V@07>=C. 4=>G0A=5 70AB>AC20==O BV0784V2 <>65 71V;LHC20B8  
9<>2V@=VABL @50:FV9 3V?5@GCB;82>ABV =0 0;>?C@8=>;.  
=B8E>;V=5@3VG=V ?@5?0@0B8 (=0?@8:;04 0B@>?V=, 1V?5@845=)  
V428I5==O 1V>4>ABC?=>ABV 4VC@5B8:V2 BV0784>2>3> @O4C ?>2O70=> 7V 7=865==O< @CE>2>W  
0:B82=>ABV (" V H284:>ABV 28?>@>6=5==O H;C=:0.  
&8B>B>:A8G=V 70A>18 (=0?@8:;04 F8:;>D>AD0  
"V07848 <>6CBL 7=86C20B8 =8@:>2V 284V;5==O F8B>B>:A8G=8E 70A>1V2 V <>6CBL ?>A8;N20B8  
AC?@5A82=C 4VN.  
!0;VF8;0B8  
@8 70AB>AC20==V 25;8:8E 4>7 A0;VF8;0BV2 3V4@>E;>@>BV0784 <>65 ?>A8;N20B8 B>:A8G=C 4VN  
A0;VF8;0BV2 =0 F5=B@0;L=C =5@2>2C A8AB5  
5B8;4>D0  
>:@5<8E 28?04:0E ?@8 A?V;L=>AC20==V 3V4@>E;>@>BV0784C V <5B8;4>D8 2V47=0G0;8 35  
<>;VB8G=C 0=5  
?>A?>@8=  
@8 >4=>G0A=>AC20==V 7 F8:;>A?>@8=0<8 ?V428ICTBLAO @878: 28=8:=5==O 3V?5@C@8:5:  
?>403@8.  
!5@F52V 3;V:>7848  
!@8G8=5=0 BV07840<8 3V?>:0;VT 3V?><03=VT@  
@5?0@0B8, 4VO O:8E 72V:  
5>1EV4=> ?5@V>48G=> :=B@>;N20B8 :=F5=B@0FVN :0;VN C ?;072V B0 ?@>2>48B8 :=B@>;L ?@8  
70AB>AC20==V :>1V=>20=>3> ?@5?0@0BC ;>70@B0=/3V4@>E;>@>BV0784 7 ?@5?0@0B0<8, 4VO  
O:8E 70;568BL 2V4 @V2=O :0;VN C ?;072V (=0?@8:;04 A5@F52V 3;V:>7848 B0 0=B80@8B18), 0 B0:>6 7  
?@5?0@0B0<8, O:V A?@8G8=ONBL «torsades de pointes» (H;C=>G:>2C B0EV:0@4VN), 2;;NG0NG8  
45O:V 0=B80@8B18, >A;V;L:8 3V?>:0;VT@G:>2>W B0EV:0@4VW.  
0=B80@8BEV=V48=, 487?>V@0  
0=B80@8B40@>=, A>B0;>;, 4>D5B8;V4, V1CB8;V4);  
45O:V 0=B8?A8E>B8G=V 70A>18 (=0?@8:;04 BV>@84078=, E;>@?@<078=, ;52<5?@<078=,  
B@VD;C>?5@078=, FV0<5<078=, AC;L?V@84, AC;LB>?@84, 0  
V=HV ?@5?0@0B8 (=0?@8:;04 15?@848;, F8A0?@84, 48D5<0=V;;, 2=CB@VH=L>25==> 22545=89  
5@8B@>D0=B@8=, ;0AB8=, ?5=B025==> 22545=89 2V=:0  
!>;V :0;LFVN



VC@5B8:8 BV0784>2>3> @O4C <>6CBL 71V;LHC20B8 220BFV :@>2V 2=0A;V4>: 7=865=>W  
5:A:@5FVW. /:I> =5>1EV4=> 70AB>A>2C20B8 ?@5?0@0B8, I> ?>?>2=NNBL 21EV4=> @53C;O@=>  
:=B@>;N20B8 @V25=L :0;LFVN 2 A8@>20BFV :@>2V V 2V4?>2V4=> 4> >B@>8<0=>3> @57C;LB0BC  
B@510 287=0G0B8 4>7C F8E ?@5?0@0BV2.  
?:82 =0 ;01>@0B>@=V ?>:07=8:8  
'5@57 2?;82 =0 <5B01>;V7< :0;LFVN BV07848 <>6CBL 2?;8=CB8 =0 @57C;LB0B8 DC=:FV>=0;L=8E  
B5ABV2 ?0@018B>284=>W 70;>78.  
0@10<075?V=  
878: A8<0B8G=>W 3V?>=0B@VT1EV4=89 ;:V=VG=89 =03;O4 70 E2>@8< B0 ;01>@0B>@=89 :=B@>;L  
:@>2V.  
>=B@0AB=V @5G>28=8, I> 4  
@8 453V4@0B0FVW, A?@8G8=5=V9 A5G>3V==8<8 70A>10<8, <>65 71V;LHC20B8AO @878:  
3>AB@>W =8@:>2>W =54>AB0B=>ABV, >A>1;82> ?@8 22545==V 25;8:8E 4>7 ?@5?0@0BV2,I> 4.  
5@54 22545==O< 9>4C =5>1EV4=> 2V4=>28B8 2>4=89 10;0=A.  
B5@8F8= (?0@5=B5@0;L=> 22545=89), :>@B8:>AB5@>W48, "B0 ?@>=>A=V 70A>18  
V4@>E;>@>BV0784 <>65 A?@8OB8 ?>@CH5==N 2>4=>-5;5:B@>;VB=>3> 10;0=AC, A?@8G8=ONG8 2  
>A=>2=>:0;VT

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

\$0@<0:>48=0

>70@B0=-3V4@>E;>@>BV0784

>2545=>, I> 7=86C20;L=0 4VO =0 0@B5@V0;L=89 B8A: :=5=BV2 ?@5?0@0BC 048B82=0, B0:8< G8=><  
:=5=B8 ?@5?0@0BC 1V;LH>NN 7=86CNBL 0@B5@V0;L=89 B8A.; 0=V6 FV :=5=B8 >:@5<.  
@8?CA:0NBL, I> FO 4VO ?>2'O70=0 7 AC<0FVTN 5D5:BV2 :=5=BV2. @V< B>3>, G5@57  
4VC@5B8G=89 5D5:B 3V4@>E;>@>BV0784 71V;LHCT 0:B82=VABL @5=V=C C ?;02V B0 284V;5==O  
0;L4>AB5@>=C, 7=86CT :=F5=B@0FVN :0;VN V 71V;LHCT @V25=L 0=3V>B5=78=C II C ?;072V. @89>  
< ;>70@B0=C 1;>:CT 2AV DV7V>;>3VG=V 5D5:B8 0=3V>B5=78=C II V 2=0A;V4>: ?@83=VG5==O  
5D5:BV2 0;L4>AB5@>=C <>65 A?@8OB8 7<5=H5==N 2B@0B8 :0;VN, ?>2O70=>W V7 70AB>AC20==O<  
4VC@5B8:0.

>70@B0= G8=8BL ?>N ?V428ICT @V25=L A5G>2>W :8A;>B8 2 :@>2V; ;<1V=0FVO ;>70@B0=C B0  
3V4@>E;>@>BV0784C ?>A;01;NT 3V?5@C@8:5

=B83V?5@B5=782=89 5D5:B ?@5?0@0BC 715@V30TBLAO ?@>B03<< 24 3>48=. =B83V?5@B5=782=89  
5D5:B 715@V30TBLAO ?@8 157?5@5@2=>AC20==V ?@5?0@0BC. @V< ACBBT2>3> 7=865==O  
0@B5@V0;L=>3> B8A:C, B5@0?VO ?@5?0@0B<< =5 G8=8;0 ;:V=VG=> 7=0GCI89 2?;82 =0 G0AB>BC  
A5@F528E A:>@>G5=L.

<<1V=0FVO ;070@B0=C V 3V4@>E;>@>BV0784C 5D5:B82=0 C 7=865==V 0@B5@V0;L=>3> B8A:C C  
G>;>2V:V2 V C 6V=>:, ?0FVT=BV2 =53@>W4=>W B0 T2@>?5>W4=>W @0A, ?0FVT=BV2 A5@54=L>3>  
(< 65 @>:V2) B0 ;VB=L>3> 2V:C (≥ 65 @>:V2), 0 B0:>6 5D5:B82=0 2 CAVE AB04VOE 0@B5@V0;L=>W  
3V?5@B5=7VW.

>70@B0=

>70@B0= F5 A8=B5B8G=89 0=B03>=VAB @5F5?B>@0 0=3V>B5=78=C II (B8? "1), I>  
70AB>A>2CTBLAO ?5@>@0;L=>. =3V>B5=78= II, ?>BC6=89 AC48=>72C6C20;L=89 70AV1, T ?5@28==8  
< 0:B82=8< 3>@<=>< @5=V=-0=3V>B5=78=>2>W A8AB5<8 V 206;828< 287=0G0;L=8< D0:B>@<  
?0B>DV7V>;>3VW 0@B5@V0;L=>W 3V?5@B5=7VW. =3V>B5=78= II 72'O7CTBLAO 7 @5F5?B>@0<8 "1  
, O:V E B:0=8=0E (=0?@8;;04 3;04:8E <'O70E AC48=, =04=8@=8:>28E 70;>70E, =8@:0E V A5@FV), V  
G8=8BL :V;L:0 206;828E 1V>;>3VG=8E 5D5:BV2, C B>:=AB@8:FVN B0 72V;L=5==O 0;L4>AB5@>=C.  
>70@B0= A5;5:B82=> 1;>:CT @5F5?B>@ AT1. C<>20E *in vitro* B0 *in vivo* ;>70@B0= V 9>3> D0@  
<0:>;>3VG=> 0:B82=89 <5B01>;VB :0@1>:A8;L=0 :8A;>B0 (E 3174) 1;>:CNBL CAV DV7V>;>3VG=>  
7=0GCIV 5D5:B8 0=3V>B5=78=C =570;56=> 2V4 465@5;0 01> H;OEC A8=B57C.

>70@B0= =5 72'O7CT V =5 1;>:CT @5F5?B>@8 V=H8E 3>@<=>V2 B0 V>==V :0=0;8, 206;82V 4;O  
@53C;OFVW 4VO;L=>ABV A5@F52>-AC48==>W A8AB5<8. @V< FL>3>, ;>70@B0= =5 2?;820T =0 4VN  
0=3V>B5=78=?5@5B2>@N20;L=>3> D5@<5=BC (:V=070 II), O:89 2V4?>2V40T 70 @>715?;5==O  
1@048:V=V=C. '5@57 I> =5 2V47=0G0NBLAO =51060=V 4VW, ?>2'O70=V 7 ?V428I5=>N  
:=F5=B@0FVTN 1@048:V=V=C. @8 22545==V ;>70@B0=C 30;LB5=78=C II =0 CB2>@5==O @5=V=C,  
I> ?@872>48BL 4> ?V428I5==O 0:B82=>ABV @5=V=C C ?;072V. V428I5==O 0:B82=>ABV @5=V=C

?@872>48BL 4> ?V428I5==O @V2=O 0=3V>B5=78=C II C ?;072V. 572060NG8 =0 FV ?V428I5==O, 0=B83V?5@B5=782=0 0:B82=VABL B0 7=865==O @V2=O 0;L4>AB5@>=C C ?;072V 715@V30NBLAO, I> 2:07CT =0 5D5:B82=5 1;>:C20==O @5F5?B>@0 0=3V>B5=78=C II. VA;O ?@8?8=5==O B5@0?VW ;>70@B0=>< 0:B82=VABL @5=V=C C ?;072V B0 :>=F5=B@0FVO 0=3V>B5=78=C ?@>BO3<> B@L>E 4=V2 ?>25@B0TBLAO 4> =>@<8.

>70@B0= B0 9>3> >A=>2=89 0:B82=89 <5B01>;VB <0NBL 28@07=VH89 0DV=VB5B 4> @5F5?B>@0 AT1, =V6 4> @5F5?B>@0 AT2. :B82=89 <5B01>;VB, 70 @>7@0EC=:0<8 >1'T<=>3> 2V4A>B:0, C 10-40 @07V2 5D5:B82=VH89, =V6 ;>70@B0=.

>70@B0= =5 2?;820T =0 02B=>=<=V @5D;5:A8 V =5 <0T B@820;>3> 2?;82C =0 @V25=L =>@04@5=0;V=C C ?;072V.

V4@>E;>@>BV0784

V4@>E;>@>BV0784 T 4VC@5B8:<< BV0784>2>3> @O4C. 5E0=V7< 0=B83V?5@B5=782=>W 4VW 4VC@5B8:0 BV0784>2>3> @O4C ?>2=VABN =52V4<89. "V07848 2?;820NBL =0 @5=0;L=89 BC1C;O@=89 <5E0=V7< 5;5:B@>;VB=>W @501A>@1FVW, B8< A0<8< 157?>A5@54=L> ?V428ICNG8 5:A:@5FVN =0B@VN B0 E;>@C C ?@81;87=> >4=0:>28E :V;L:>ABOE. VC@5B8G=89 2?;82 3V4@>E;>@>BV0784C 7=86CT >1'T< ?;07<8, ?V428ICT 0:B82=VABL @5=V=C C ?;07AB5@>=C 7 ?>A;V4>2=8< 7@>AB0==O< ?>:07=8:V2 :0;VN 2 A5GV V 2B@0B>N 1V:0@1=>0BC B0 7=865==O< @V2=O :0;VN 2 A8@>20BFV. >6;82>, G5@57 1;>:04C @5=V=-0;L4>AB5@>=>2>W A8AB5<8 AC?CB=T ?@87=0G5==O 0=B03>=VABV2 @5F5?B>@V2 0=3V>B5=78=C II A?@80T >1>@>B=V9 2B@0BV :0;VN, ?>2'O70=V9 7 4VC@5B8:<< BV0784>2>3> @O4C.

VA;O ?5@>@0;L=>3> ?@89>7?>G8=0TBLAO ?@>BO3<> 42>E 3>48=, 4>AO30T ?V:C ?@>BO3<> 4 3>48= V B@820T ?@>BO3<> 6-12 3>48=. =B83V?5@B5=782=89 5D5:B B@820T =5 1V;LH5 24 3>48=. \$0@<0:>:V=5B8:0.

A<>:BC20==O.

>70@B0=

VA;O ?5@>@0;L=>3> 70AB>AC20==O ;>70@B0= 4>1@5 2A<>:BCTBLAO V 707=0T ?5@28==>3> <5B01>;V7@5==O< >4=>3> 0:B82=>3> :0@1>:A8;L=>3> <5B01>;VBC B0 V=H8E D0@<0:>;>3VG=> =50:B82=8E <5B01>;V BV2. !8AB5<=0 1V>4>ABC?=VABL ;>70@B0=C AB0=>28BL ?@81;87=> 33 %. 0:A8 <0;L=0 :>=F5=B@0FVO ;>70@B0=C B0 9>3> 0:B82=>3> <5B01>;VBC 4>AO30TBLAO ?@81;87=> G5@57 3>48=C V G5@57 3-4 3>48=8 ?VA;O ?@89>2V4=>. @89<< W6V =5 A?@8G8=OT ;V=VG=> 7=0GCI8E 2V4E8;5=L D0@<0:>:V=5B8G=>3> ?@>DV;N.

>7?>4V;

>70@B0=

V;LH5 99 % ;>70@B0=C B0 9>3> 0:B82=>3> <5B01>;VBC 72'O7CTBLAO 7 1V;;0<8 ?;07<8 :@>2V, ?5@5206=> 7 0;L1C34 ;. # 4>A;V465==V =0 IC@0E ;>70@B0= =525;8:>N N 01> 7>2AV< =5 ?@>=8:02 G5@57 35<0B>5=F5D0;VG=89 10@'T@.

V4@>E;>@>BV0784

V4@>E;>@>BV0784 ?@>=8:0T :@V7L ?;0F5=B0@=89 10@T@, =5 ?@>=8:0T :@V7L 35 <0B>5=F5D0;VG=89 10@'T@; ?@>=8:0T C 3@C4=5 <>;>:.

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

>70@B0=

@81;87=> 14 % ?5@>@0;L=> 01> 2=CB@VH=L>25==> 22545=>W 4>78 ;>70@B0=C <5B01>;V7CTBLAO C 9>3> 0:B82=89 <5B01>;VB. VA;O ?5@>@0;L=>3> 01> 2=CB@VH=L>25==>3> 22545==O, ?>7=0G5=>3> @04V>0:B82=8< 2C3V;;O< (14C) ;>70@B0=C :0;VN, @04V>0:B82=VABL ?;07<8 :@>2V A?@8G8=5=0 2 >A=>2=>70@B0=>< B0 9>3> 0:B82=8< <5B01>;VB>A;V465=8E >AV1 ;>70@B0= BV;L:8 =57=0G=>NN ?5@5B2>@NTBLAO =0 0:B82=89 <5B01>;VB. @V< 0:B82=>3> <5B01>;VBC, D>@

82545==O

>70@B0=

;V@5=A ;>70@B0=C B0 9>3> 0:B82=>3> <5B01>;VBC 7 ?;07<8 :@>2V 2V4?>2V4=> AB0=>28BL ?@81;87=> 600 <;E2 B0 50 <;E2. ;V@5=A ;>70@B0=C B0 9>3> 0:B82=>3> <5B01>;VBC 7 =8@>; ?@81;87=> AB0=>28BL 2V4?>2V4=> 74 <;E2 V 26 <;E2. @8 ?5@>@0;L=>48BLAO 4 % 70AB>A>20=>W 4>78 ;>70@B0=C C =573> <5B01>;VBC.

\$0@<0:>:V=5B8G=V 2;0AB82>ABV ;>70@B0=C B0 9>3> 0:B82=>3> <5B01>;VBC ;V=V9=> 7AC20==V  
?5@>@0;L=8E 4>7 ;>70@B0=C :0;VN 4> 200 <3.

VA;O ?5@>@0;L=>3> ?@89>F5=B@0FVW ;>70@B0=C B0 9>3> 0:B82=>3> <5B01>;VBC C ?;072V 7  
<5=HCNBLAO ?>;V5:A?>=5=FV0;L=>; ?5@V>4 =0?V2282545==O AB0=>28BL ?@81;87=> 2  
3>48=8 B0

6-9 3>48= 2V4?>2V4=>. @8 >4=>@07>2>7C20==V 100 <3 =0 4>1C 0=V ;>70@B0=, 0=V 9>3> 0:B82=89  
<5B01>;VB VAB>B=> =5 =0:>?8GCNBLAO C ?;072V.

1V;V0@=0, V =8@:>20 5:A:@5FVO 2V4V3@0NBL @>;L 2 5;V70@B0=C B0 9>3> 0:B82=8E  
<5B01>;VBV2. VA;O ?@89> ?5@>@0;L=>W 4>78 ?>7=0G5=>3> @04V>0:B82=8< 2C3V;;O< (14C)

35 % @04V>0:B82=>ABV 28O2;ONBL C A5GV, 0 58 % C D5:0;VOE.

V4@>E;>@>BV0784

V4@>E;>@>BV0784 =5 <5B01>;V7CTBLAO, 0;5 H284:> 282>48BLAO =8@:0<8. >;8 :>=F5=B@0FVW  
?@5?0@0BC C ?;072V :>=B@>;N20;8 ?@>BO3<< ?@8=09<=V 24 3>48=, ?5@V>4 =0?V2282545==O 7 ?;07  
<8 :>2V 3V4@>E;>@>BV0784C AB0=>282 5,6-14,8 3>48=8. @8=09<=V 61 % ?5@>@0;L=>W 4>78  
282>48BLAO C =57BO3<< 24 3>48=8.

%0@0:B5@8AB8:8 C ?0FVT=BV2

>70@B0=-3V4@>E;>@>BV0784

>=F5=B@0FVW ;>70@B0=C B0 9>3> 0:B82=>3> <5B01>;VBC C ?;072V B0 2A<>:BC20==O  
3V4@>E;>@>BV0784C C ?0FVT=BV2 ;VB=L>3> 2V:C 7 0@B5@V0;L=>N 3V?5@B5=7VTN 7=0G=> =5  
2V4@V7=ONBLAO 2V4 B8E, I> A?>AB5@V30NBLAO C <>;>48E ?0FVT=BV2 7 0@B5@V0;L=>N  
3V?5@B5=7VTN.

>70@B0=

VA;O ?5@>@0;L=>3> 70AB>AC20==O ?0FVT=B0< 7 0;:>3>;L=8< F8@>7<< ?5GV=:8 ;53:>3> B0 ?>3>  
ABC?5=O BO6:>ABV :>=F5=B@0FVW ;>70@B0=C B0 9>3> 0:B82=8E <5B01>;VBV2 C ?;072V 1C;8  
2V4?>2V4=> C 5 B0 C 1,7 @070 28I8<8, =V6 C <>;>48E 2>;>=B5@V2.

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

A=>2=V DV78:>-EVABV: 6>2BV, >20;L=V, 45I> 42>>?C;V B01;5B:8, 2:@8BV ?;V2:>2>N >1>;>=:N7  
@8A:>N 7 >4=>3> 1>:C.

"5@ABV.5 @>:V2.

#<>28 715@V30==O.

15@V30B8 ?@8 B5 C 2 >@83V=0;L=V9 C?0:>2FV 4;O 70E8ABC 2V4 2>;>38. 15@V30B8 C =54>ABC?=>

#?0:>2:0. > 10 B01;5B>: C 1;VAB5@V; ?> 3, 01> ?> 6, 01> ?> 9 1;VAB5@V2 C :0@B>==V9 :>@>1FV;  
> 14 B01;5B>: C 1;VAB5@V; ?> 1, 01> ?> 2, 01> ?> 4, 01> ?> 6, 01> ?> 7 1;VAB5@V2 C :0@B>==V9  
:>@>1FV.

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

8@>1=8:.

, 4.4., >2> <5AB>, !;>25=VO/

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**VAF57=0E>465==O.**

(<0@TH:0 F5AB0 6, 8501 >2> <5AB>, !;>25=VO/  
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