

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

®
(EGLONYL®)

!;:04:

4VNG0 @5G>28=0: AC;L?V@84;

1 :0?AC;0 AC;L?V@84C 50 <3;

4>?>28=8: ;0:B>78 <>=>3V4@0B, <5B8;F5;N;>70, B0;L:, <03=VN AB50@0B, >1>;=>:0 :0?AC;8: 65;0B8=, B8B0=C 4V>:A84 (171).

V:0@AL:0 D>@<0. □0?AC;8.

A=>2=V DV78:>-EVABV: =5?@>7>@V 1V;V 01><0965 1V;V :0?AC;8 4, I>

\$0@<0:>B5@0?52B8G=0 3@C?0. =B8?A8E>B8G=V 70A>18. >4 "% N05A L01.

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

\$0@<0:>48=0

!C;L?V@84 2?;820T =0 4>?02C ?5@540GC 2 3>;>2=>:8E 4>70E AC;L?V@84 B0:>6 7<5=HCT

?@>4C:B82=C A8<0B8:C.

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

VA;O ?5@>@0;L=>3> 22545==O >4=VTW :0?AC;8 50<3 ?V:>20 :>=F5=B@0FVO AC;L?V@84C 2 ?;07 V>4>ABC?=VABL ?5@>@0;L=8E ;V:0@AL:8E D>@< AB0=>28BL 25-35 % 7 H8@>:8<8 V=482V4C0;L=8 <8 :>;820==O<8; AC;L?V@84 <0T ;V=V9=89 D0@<0:>=V=5B8G=89 ?@>DV;L ?VA;O 22545==O C 4>70E 2V4 50 4> 300 <3.

!C;L?V@84 H284:> @>7?>4V;OTBLAO 2 B:0=8=0E >@30=V728BL 0,94 ;/:3. 207C20==O 7 ?@>B5W=0<8 ?;07<8 AB0=>28BL 40 %.

!C;L?V@84 C =57=0G=8E :V;L:>ABOE 28O2;OTBLAO 2 3@C4=>

!C;L?V@84 ?@0:B8G=> =5 <5B01>;V7CTBLAO 2 >@30=V7

!C;L?V@84 282>48BLAO 2 >A=>2=> AB0=>28BL 126<;/E2. 5@V>4 =0?V2282545==O 7 ?;07<8 7 3>48=.

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

>:070==O. >@>B:>B@820;5 A8<0B8G=5 ;V:C20==O B@82>6=8E AB0=V2 C 4>@>A;8E, C @07V, :>;8 728G09=V B5@0?52B8G=V 70E>48 =5 40;8 @57C;LB0BV2.

!5@9>7=V ?>254V=>2V @>7;048 (068B0FVO, A0<?>H:>465==O, AB5@5>B8?VO) C 4VB59 2V:< 2V4 6 @>:V2, >A>1;82> C ?0FVT=V2 7 0CB8G=8<8 A8=4@<0<8.

@>B8?>:070==O.

- V428I5=0 GCB;82VABL 4> AC;L?V@84C 01> 1C4L-O:>W 7 4>?>28= ?@5?0@0BC.

- @>;0:B8=>70;56=V ?CE;8=8 (=0?@8;;04 ?@>;0:B8=>A5:@5BCNG0 045=><0 3V?>DV70 (?@>;0:B8=><0) B0 @0: <>;>G=>W 70;>78).

- □V4><89 01> ?V4>7@N20=89 4V03=>7 D5>E@><>F8B><8.

- >AB@0 ?>@DV@VO.

- □><1V=0FVW 7 =50=B8?0@:V=A>=VG=8<8 03>=VAB0<8 4>?0;V=, @>B83>B8= B0 :V=03>;V4), :><1V=0FVW 7 ;52>4>?>N 01> 0=B8?0@:V=A>=VG=8<8 ;V:0@AL:8<8 70A>10<8 (2;;NG0NG8 @>?V=>@>), :><1V=0FVW 7 <5EVB078=><, F8B0;>?@0<< B0 5AF8B0;>?@0<< (482. @>74V; «70T <>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9»).

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

!540B82=V 70A>18

!;V4 ?0<OB0B8, I> 1030B> ;V:0@AL:8E 70A>1V2 <>6CBL 28O2;OB8 048B82=89 30;L2C A8AB548B8 4> 7 <5=H5==O @>7C<>2>W 0:B82=>ABV. &V 70A>18 2;;NG0NBL ?>EV4=V<>@DV=C (0=0;35B8:8, 70A>18 2V4 :0H;N B0 70;5?B8G=V 70A>18, 10@1VBC@0B8, 15=7>4V075?V=8, =515=7>4V075?V=>2V 0=:AV>;VB8G=V 70A>18 (B0:V O:<5?@>10<0B), 3V?=>B8G=V 70A>18, A540B82=V 0=B845?@5A0=B8 (01-0=B83VAB0N 4VTN, 10;;>D5= V B0;V4>

@5?0@0B8, O:V <>6CBL A?@8G8=8B8 @>728B>: ?0@>:A87<0;L=>W H;C=>G:>2>W B0EV:0@4VW
(torsades de pointes)
> FL>3> A5@9>7=>3> ?>@CH5==O A5@F52>3> @8BW 0:B82=>ABV. @>2>:CNG8<8 D0:B>@0<8 T
3V?>:0;VT<1V=0FVW, ?@87=0G5==O O:8E 28<030T >15@56=>ABV (7 :0;V9=5715@V30NG8<8
?@5?0@0B0<8)) B0 1@048:0@4VO (482. <<><1V=0FVW, ?@87=0G5==O O:8E 28<030T >15@56=>ABV (7
?@5?0@0B0<8, O:V A?@8G8=ONBL 1@048:0@4VN)) 01> =0O2=VABL 2@>465=>3> 01> =01CB>3>
?>4>265==O V=B5@20;C QT.
> B0:8E 70A>1V2 =0;560BL, 7>:@5<0, 0=B80@8B;5?B8:8.
B0:C 270T<>4VN 2ABC?0NBL 5@8B@>4>;0A5B@>=, A?V@0@<0E 4;O 2=CB@VH=L>25==>3>
22545==O.
!C?CB=T 22545==O 42>E ?@5?0@0BV2, I> <>6CBL A?@8G8=8B8 ?0@>:A87<0;L=C H;C=>G:>2C
B0EV:0@4VN (torsades de pointes) 7030;< ?@>B8?>:070=5. @>B5 28=OB>: AB0=>2;OBL <5B04>= B0
45O:V V=HV @5G>28=8:
?@>B8?0@078B0@>=V 70A>18 (30;>D0=B@8=, ;N<5D0=B@8=, ?5=B0 :<<1V=C20B8 7 V=H8<8
?@5?0@0B0<8, O:V <>6CBL A?@8G8=8B8 ?0@>:A87<0;L=C H;C=>G:>2C B0EV:0@4VN B8?C
«?V@C5B» (torsades de pointes);
=59@>;5?B8:8, O:V <>6CBL A?@8G8=8B8 ?0@>:A87<0;L=C H;C=>G:>2C B0EV:0@4VN B8?C
«?V@C5B» (torsades de pointes), B0:>6 =5 @5:<5=4CNBLAO, 0;5 =5 ?@>B8?>:070=V 4;O
70AB>AC20==O 2 :<<1V=0FVW 7 V=H8<8 ?@5?0@0B0<8, O:V <>6CBL 7C<>28B8 @>728B>: ?0@>:A87
<0;L=>W H;C=>G:>2>W B0EV:0@4VW B8?C «?V@C5B» (torsades de pointes).
@>B8?>:070=V :<<1V=0FVW (482. @>74V; «@>B8?>:070==O»)).
?>?@0<, 5AF8B0;>?@0<
V428I5=89 @878: @>728B:C H;C=>G:>28E 0@8BA>1;82> ?>;V<>@D=>W H;C=>G:>2>W B0EV:0@4VW.
3>=VAB8 4>D028E @5F5?B>@V2 =5 4;O ;V:C20==O E2>@>18 0@:V=A>=0 (:015@3>;V=, EV=03>;V4,
@>B83>B8=)
V6 03>=VAB0<8 4>D0;5?B8:0<8 VA=CT 270T<=89 0=B03>=V7
52>4>?0 B0 0=B8?0@:V=A>=VG=V ?@5?0@0B8 (2;:NG0NG8 @>?V=>@>);
V6 ;52>4>?>N, 0=B8?0@:V=A>=VG=8<8 ?@5?0@0B0<8 (0<0=B048=, 0?><>@DV=, 1@><>:@8?B8=,
5=B0:0?>=, ;V7C@84, ?5@3>;V4, ?V@81548;, ?@0;, @>?V=>@>;, @0703V;V=, A5;53V;V=) B0
=59@>;5?B8:0<8 VA=CT 270T<=89 0=B03>=V7
3>=VAB8 4>?0=VAB0<8 4>?01EV4=5 ?@87=0G5==O =59@>;5?B8:V2, 4>78 03>=VABV2 4>?0ABC?>2>
7=878B8 (@V7:0 WE 2V4O:VA=>3> =59@>;5?B8G=>3> A8=4@>A:V;L:8 >4=>G0A=5 70AB>AC20==O
?@5?0@0BV2 ?@>B8?>:070=5.
5EVB078=
V428I5=89 @878: @>728B:C H;C=>G:>28E 0@8BA>1;82> ?>;V<>@D=>W H;C=>G:>2>W B0EV:0@4VW.
51060=V :<<1V=0FVW (482. @>74V; «A>1;82>ABV 70AB>AC20==O»)).
?@>B8?0@078B0@>=8<8 ?@5?0@0B0<8, O:V <>6CBL A?@8G8=8B8 @>728B>: ?0@>:A87<0;L=>W
H;C=>G:>2>W B0EV:0@4VW (torsades de pointes) (30;>D0=B@8=, ;N<5D0=B@8=, ?5=B0V428I5=89
@878: H;C=>G:>28E 0@8B7>:@5<0 ?0@>:A87<0;L=>W H;C=>G:>2>W B0EV:0@4VW B8?C «?V@C5B»)
(torsades de pointes). /:I> <>6;82>, ;V:C20==O ?@>B83@81:>28<8 07>;0<8 A;V4 ?@878=8B8.
/:I> >4=>G0A=>3>;V:C20==O C=8:=CB8 =5 <>6=0, ?5@54 9>3> ?>G0B:<< ?>B@V1=> >FV=8B8 =0
AB0= QT-V=B5@20;C B0 2 9>3> E>4V :=B@>;N20B8 ?>:07=8:8 .
V=H8<8 ?@5?0@0B8, O:V <>6CBL 7C<>28B8 ?0@>:A87<0;L=C H;C=>G:>2C B0EV:0@4VN B8?C
«?V@C5B» (torsades de pointes) (0=B80@8BEV=V48=, 487>?V@040@>=, 4@>=540@>=, A>B0;>;,
4>D5B8;V4, V1CB8;V4) B0 V=HV ?@5?0@0B8, B0:V O: 15?@848;, F870?@84, 48D5<0=V;; 4>;0A5B@>=,
5@8B@>4;O 2=CB@VH=L>25==>3> 22545==O, ;52>D;>:A0F8=, ;0AB8=, ?@C:0;>?@84, 2V=:04;O
2=CB@VH=L>25==>3> 22545==O, <>:A8D;>:A0F8=, A?V@04;O 2=CB@VH=L>25==>3> 22545==O
B0 B>@0
8A>:89 @878: H;C=>G:>28E 0@8B:@5<0 ?0@>:A87<0;L=>W H;C=>G:>2>W B0EV:0@4VW B8?C
«?V@C5B» (torsades de pointes).
V=H8<8 =59@>;5?B8:0<8, O:V <>6CBL A?@8G8=8B8 @>728B>: ?0@>:A87<0;L=>W H;C=>G:>2>W
B0EV:0@4VW B8?C «?V@C5B» (torsades de pointes) (0@?@><078=, FV0<5<078=, 4@>?5@84>;,
D;C?5=B8:A>;, D;CD5=078=, 30;>?5@84>;, ;52><5?@><078=, ?V<>784, ?V?>BV0784, A5@B8=4>;,
AC;L?V@84, AC;LB>?@84, BV0?@84, 25@0;V?@84, 7C:;>?5=B8:A>;)

8A>:89 @878: 28=8:=5==O H;C=>G:>28E 0@8B:@5<0 ?0@>:A87<0;L=>W H;C=>G:>2>W B0EV:0@4VW B8?C «?V@C5B» (torsades de pointes).

5B0=>;><

>B5=FVN20==O A540B82=8E 5D5:BV2 =59@>;5?B8G=8E 70A>1V2.

0FVT=B8 ?>28==V C=8:0B8 26820==O 0;:>3>;L=8E =0?>W2 01> 70AB>AC20==O ;V:0@AL:8E 70A>1V2, O:V 289 A?8@B.

<5B04>=><

V428I5=89 @878: H;C=>G:>28E 0@8B:@5<0 ?0@>:A87<0;L=>W H;C=>G:>2>W B0EV:0@4VW B8?C «?V@C5B» (torsades de pointes).

><1V=0FVW, ?@87=0G5==O O:8E 28<030T >15@56=>ABV

78B@>

V428I5=89 @878: @>728B:C H;C=>G:>28E 0@8BA>1;82> ?>;V<>@D=>W H;C=>G:>2>W B0EV:0@4VW. ?5@V>4 >4=>G0A=>3> 70AB>AC20==O =5>1EV4=> 28:>=C20B8 B0 74V9A=N20B8 ;;V=VG=89

:>=B@>;L.

15B0-1;:>:0B>@0<8, O:V 70AB>A>2CNBLAO ?@8 A5@F52V9 =54>AB0B=>ABV (1VA>?@>;>;, :0@2548;>;, <5B>?@>;>;, =51V2>;>;)

V428I5=89 @878: H;C=>G:>28E 0@8B:@5<0 ?0@>:A87<0;L=>W H;C=>G:>2>W B0EV:0@4VW B8?C «?V@C5B» (torsades de pointes). 5>1EV4=89 ;;V=VG=89 <>=VB>@8=3 B0 :>=B@>;L .

?@5?0@0B0<8, O:V A?@8G8=ONBL 1@048:0@4VN (B0:8<8 O: 0=B80@8B:0B>@8, 45O:V 0=B80@8B :0B>@8 :0;LFVT28E :0=0;V2 (48;BV075<, 25@0?0=V48=, 3C0=D0F8=), 3;V:>7848 483VB0;VAC, ?V;>:0@?V=, 0=B8E>;V=5AB5@07=V 70A>18)

V428I5=89 @878: H;C=>G:>28E 0@8B:@5<0 ?0@>:A87<0;L=>W H;C=>G:>2>W B0EV:0@4VW B8?C «?V@C5B» (torsades de pointes). 5>1EV4=89 ;;V=VG=89 <>=VB>@8=3 B0 :>=B@>;L .

;0@8B@>

V428I5=89 @878: @>728B:C H;C=>G:>28E 0@8BA>1;82> ?>;V<>@D=>W H;C=>G:>2>W B0EV:0@4VW. ?5@V>4 >4=>G0A=>3> 70AB>AC20==O =5>1EV4=> 28:>=C20B8 B0 74V9A=N20B8 ;;V=VG=89

:>=B@>;L.

:0;V9=5715@V30NG8<8 ?@5?0@0B0<8 (:0;V9=5715@V30NGV 4VC@5B8:8, A0<>ABV9=> 01> 2 :> <1V=0FVW, AB8=>A=V 70A>18, 3;N:>:>@B8:>W48, B5B@0:>70:B84 V 0B5@8F8= 4;O

2=CB@VH=L>25==>3> 70AB>AC20==O)

V428I5=89 @878: H;C=>G:>28E 0@8B:@5<0 ?0@>:A87<0;L=>W H;C=>G:>2>W B0EV:0@4VW B8?C «?V@C5B» (torsades de pointes).

5@54 22545==O< A;V4 ?@>25AB8 :>@5:FVN =0O2=>W 3V?>:0;VT

@5?0@0B8 ;VBVN

878: ?>O28 =59@>?A8EV0B@8G=8E >7=0.; O:V 2:07CNBL =0 7;>O:VA=89 =59@>;5?B8G=89 A8=4@< 01> >B@CT==O ;VBVT

5>1EV4=> @53C;O@=> :>=B@>;N20B8 ;;V=VG=C :0@B8=C B0 @57C;LB0B8 ;01>@0B>@=8E

0=0;V7V2, >A>1;82> =0 ?>G0B:C >4=>G0A=>3> 70AB>AC20==O.

0AB>AC20==O ;VBVN ?V428ICT @878: 28=8:=5==O 5:AB@0?V@01VG=8E @50:FV9.

>:A8B@>

V428I5=89 @878: @>728B:C H;C=>G:>28E 0@8BA>1;82> ?>;V<>@D=>W H;C=>G:>2>W B0EV:0@4VW. ?5@V>4 >4=>G0A=>3> 70AB>AC20==O =5>1EV4=> 28:>=C20B8 B0 74V9A=N20B8 ;;V=VG=89

:>=B@>;L

7 AC:@0;D0B><

<5=H5==O 01A>@1FVW AC;L?V@84C 2 H;C=:>2>-.8H:>2>

V6 22545==O< AC:@0;D0BC B0 AC;L?V@84C <0T 1CB8 ?52=89 V=B5@20; G0AC (1V;LH5 2 3>48=, O:I> F5 <>6;82>).

VH;C=:>2>-.8H:>28<8 70A>10<8 W 4VW, 0=B0F840<8 B0 0:B82>20=8< 2C3V;;O<

<5=H5==O 01A>@1FVW AC;L?V@84C 2 H;C=:>2>-.8H:>2>

V6 22545==O< F8E 035=BV2 V AC;L?V@84C <0T 1CB8 ?52=89 V=B5@20; G0AC (1V;LH5 2 3>48=, O:I> F5 <>6;82>).

><1V=0FVW, O:V A;V4 27OB8 4> C2038

=HV A540B82=V 70A>18

V;LH 28@065=5 ?@83=VG5==O DC=:FVW F5=B@0;L=>W =5@2>2>W A8AB5<8. '5@57 ?>3V@H5==O
740B=>ABV 4> :>=F5=B@0FVW C2038 :5@C20==O B@0=A?>@B=8<8 70A>10<8 B0 @>1>B0 7 V=H8<8
<5E0=V7<0<8 <>6CBL 1CB8 =5157?5G=8<8.

=B83V?5@B5=782=V 70A>18

V428I5==O @878:C 0@B5@V0;L=>W 3V?>B5=7VW, >A>1;82> >@B>AB0B8G=>W.

15B0-1;>:0B>@0<8 (:@V< 5A<>;>;C, A>B0;>;C B0 15B0-1;>:0B>@V2, I> 70AB>A>2CNBL E2>@V V7
A5@F52>N =54>AB0B=VABN)

!C48=>@>7H8@N20;L=0 4VO V @878: 3V?>B5=7VW, 7>:@5<0 ?>ABC@0;L=>W (048B82=89 5D5:B).

=VB@0B0<8, =VB@8B0<8 B0 A?>@V4=5=8<8 ?@5?0@0B0<8

V428I5=89 @878: 3V?>B5=7VW, 7>:@5<0 ?>ABC@0;L=>W.

!C;L?V@84 <>65 7=860B8 5D5:B82=VABL @>?V=>@>;C.

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

?0FVT=BV2, O:V E2>@VNBL =0 FC:@>289 4V015B 01><0NBL D0:B>@8 @878:C @>728B:C
FC:@>2>3> 4V015BC, =0 ?>G0B:C B5@0?VW AC;L?V@84< A;V4 28:>=C20B8 =0;56=89 :>=B@>;L
@V2=O 3;N:>78 2 :@>2V.:@V<>A>1;828E 28?04:V2, F59 ;V:0@AL:89 70AV1 =5 A;V4 ?@87=0G0B8
?0FVT=B0< 7 E2>@>1>N 0@:V=A>=0.

;O ?0FVT=BV2 7 =8@:>2>N =54>AB0B=VABN @5:<5=4CTBLAO 7<5=H5=5 4>7C20==O B0 ?>A8;5=89
<=>VB>@8=3; C @07V A5@9>7=>W =8@:>2>W =54>AB0B=>ABV 1060=> ?@>2>48B8
?5@5@82G0ABV :C@A8 ;V:C20==O.

V4 G0A ;V:C20==O AC;L?V@84< =5>1EV4=5 @5B5;L=VH5 A?>AB5@565==O 4;O: E2>@8E =0
5?V;5?AVN, >A:V;L:8 AC;L?V@84<>65 7=86C20B8 AC4<=89 ?>@V3; 1C;8 ?>2V4<<;5==O ?@> 28?04:8
28=8:=5==O AC4< C ?0FVT=BV2, O:V ;V:C20;8AO AC;L?V@84< (482. @>74V; <>1VG=V @50:FVW»),
?0FVT=BV2 ;VB=L>3> 2V:C, O:V T A?@89=OB;82VH8<8 4> @>728B:C ?>ABC@0;L=>W 3V?>B5=7VW,
A540B82=>3> 2?;82C B0 5:AB@0?V@0

?0FVT=BV2 7 03@5A82=>N ?>254V=>N 01> 068B0FVTN 7 V28=5= ?@87=0G0B8AO @07<< V7
A540B82=8<8 70A>10<8.

>2V4><;O;>AO, I> =0 D>=V 70AB>AC20==O 0=B8?A8E>B8:V2, C B>=V;®, 28=8:0;8 ;59:>?5=VO,
=59B@>?5=VO B0 03@0=C;>F8B>7. =D5:FVW =52AB0=>2;5=>W 5BV>;>3VW 01> ?V428I5==O B5
2;5=>W 5BV>;>3VW <>6CBL 1CB8 >7=0:0<8 ;59:>?5=VW (482. @>74V; <>1VG=V @50:FVW»): 2 B0:8E
28?04:0E A;V4 =5309=> 28:>=0B8 0=0;V7 :@>2V.

>B5=V9=> ;5B0;L=89 7;>O:VA=89 =59@>;5?B8G=89 A8=4@> # @07V ?V428I5==O B5
=57OA>20=>W 5BV>;>3VW ;V:C20==O =5>1EV4=> =5309=> ?@8?8=8B8, >A:V;L:8 F5<>65 1CB8 >4=8<
V7 A8O:VA=>3> A8=4@>(1;V4VABL, 3V?5@B5@=><=V @>7;048, ?>@CH5==O A2V4<>ABV,
@83V4=VABL<□O7V2).

7=0:8 48ADC=:FVW 2535B0B82=>W =5@2>2>W A8AB5<8, B0:V O: ?>A8;5=0 ?VB;82VABL V 7>
B8A:C, <>6CBL @>72820B8AO 4> ?>O28 3V?5@B5@

%>G0 F59 5D5:B =59@>;5?B8:V2 <>65 <0B8 V4V>A8=:@0B8G=C ?@8@>4C, <>6CBL 1CB8 ?@8ACB=V
D0:B>@8 @878:C, B0:V O: 7=52>4=5==O B0 >@30=VG=5 CH:>465==O <>7:C.

>4>265==O V=B5@20;C QT. !C;L?V@84 <>65 ?@872>48B8 4> 70;56=>3> 2V4 4>78 ?>4>265==O

V=B5@20;C QT. &59 5D5:B, O:89, O: 2V4<>, ?V428ICT @878: @>728B:C A5@9>7=8E

25=B@8:C;O@=8E 0@8B:@5<0 ?0@>:A87<0;L=>W H;C=>G:>2>W B0EV:0@4VW B8?C «?V@C5B»,
G0ABVH5 A?>AB5@V30TBLAO C ?0FVT=BV2 7 1@048:0@4VTN, 3V?>:0;VT465=8< 01> =01CB8<
?>4>265==O< V=B5@20;C QT (:>;8 AC;L?V@84 ?@89<0TBLAO >4=>G0A=> 7 ;V:0@AL:8< 70A>1><,
O:89 ?@872>48BL 4> ?>4>265==O V=B5@20;C QT) (482. @>74V; <>1VG=V @50:FVW»).

2060NG8 =0 F5, ?5@H =V6 22>48B8 ?@5?0@0B V O:I> 4>72>;OT ;;V=VG=0 A8BC0FVO, A;V4
?5@52V@8B8 =0O2=VABL C ?0FVT=BV2D0:B>@V2 @878:C, O:V <>6CBL A?@8OB8 @>728B:C
FL>3> B8?C 0@8B465=5 ?>4>265==O V=B5@20;C QT, AC?CB=T ;V:C20==O ;V:0@AL:8< 70A>1><, O:89
<>65 A?@8G8=OB8 28@065=C 1@048:0@4VN (<5=H =V6 55 C40@V2 70 E28;8=C), 3V?>:0;VT
2V;L=5==O 2=CB@VH=L>A5@F52>W ?@>2V4=>ABV 01> ?>4>265==O QT-V=B5@20;C (482. @>74V;8
«@>B8?>:070==O» B0 <□70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9»).

0 28=OB:>< =52V4:;04=8E 28?04:V2, @5:><5=4CTBLAO ?@>25AB8 -4>A;V465==O ?V4 G0A
>?G0B:>2>3> >1AB565==O ?0FVT=BV2, O:V ?>28==V >B@8;V:C20==O =59@>;5?B8G=8< ?@5?0@0B>
=AC;LB
V4 G0A @0=4>20=8E ?;0F51>.:>=B@>;L>20=8E ;:V=VG=8E 4>A;V465=L C ?0FVT=BV2 ;VB=L>3> 2V:C
7 45<5=FVTN, O:V ;V:C20;8AO 45O:8<8 0B8?>28<8 0=B8?A8E>B8G=8<8 70A>10<8, A?>AB5@V30;8
?V428I5=89 @878: V=AC;LBC ?>@V2=O=> 7 B8<8, EB> >B@8. 5E0=V7< FL>3> ?V428I5==O @878:C
=52V4><89. 5 <6=0 28:;NG0B8 VA=C20==O ?V428I5=>3> @878:C ?@8 70AB>AC20==V V=H8E
0=B8?A8E>B8G=8E ?@5?0@0BV2 01> 2 V=H8E ?>?C;OFVOE ?0FVT=BV2. 0FVT=B0<, O:V <0NBL
D0:B>@8 @878:C V=AC;LBC, F59 ;V:0@AL:89 70AV1 ?@87=0G0NBL 7 >15@56=VABN
0FVT=B8 ;VB=L>3> 2V:C 7 45<5=FVTN
878: A<5@BV ?V428ICTBLAO A5@54 ?0FVT=BV2 ;VB=L>3> 2V:C 7 ?A8E>7<, A?@8G8=5=8< 45
<5=FVTN, O:V >B@8B8G=8<8 70A>10<8.
=0;V7 40=8E 17 ?;0F51>.:>=B@>;L>20=8E 4>A;V465=L (V7 A5@54=L>N B@820;VABN 10 B86=V2), O:V
?@>2>48;8AL 70 CG0ABN ?0FVT=BV2, I>, 7030;><, ?@89<0;8 0B8?>2V 0=B8?A8E>B8G=V 70A>18,
?>:0702, I> @878: A<5@BV 71V;LH82AO C 1,6 1,7 @070 A5@54 ?0FVT=BV2, O:V ?@89<0;8 FV
?@5?0@0B8, ?>@V2=O=> 7 ?;0F51>.
VA;O 7025@H5==O A5@54=L>3> B5@B@8202 10 B86=V2, @878: A<5@BV AB0=>282 4,5 % C 3@C?V
?0FVT=BV2, O:V >B@8@V2=O=> 7 2,6 % C 3@C?V ?;0F51>.
%>G0 ?@8G8=8 A<5@BV ?V4 G0A ;:V=VG=8E 4>A;V465=L V7 70AB>AC20==O< 0B8?>28E
0=B8?A8E>B8G=8E 70A>1V2 1C;8 @V7=8<8, 1V;LHVABL A<5@B59 =0AB020;0 2=0A;V4>: 01>
A5@F52>-AC48==8E (B0:8E O: A5@F520 =54>AB0B=VABL, @0?B>20 A<5@BL), 01> V=D5:FV9=8E
70E2>@N20=L (=0?@8:;04 ?=52<>=VW).
?V45;>3VG=V 4>A;V465==O A2V4G0BL ?@> B5, I> ;V:C20==O AB0=40@B=8<8 0=B8?A8E>B8G=8<8
70A>10<8 <65 71V;LHC20B8 A<5@B=VABL B0: A0<>, O: V C @07V 70AB>AC20==O 0B8?>28E
0=B8?A8E>B8G=8E 70A>1V2.
V4?>2V4=0 @>;L 0=B8?A8E>B8G=>3> 70A>1C B0 E0@0:B5@8AB8: ?0FVT=B0 C ?V428I5==V @V2=O A
<5@B=>ABV 2 5?V45;>3VG=8E 4>A;V465==OE 70;8H0TBLAO =5287=0G5=>N.
5=>7=0 B@><I>5<I>;VO. V4 G0A 70AB>AC20==O 0=B8?A8E>B8G=8E 70A>1V2 ?>2V4<>;O;>AO
?@> V=>4V ;5B0;L=V 28?04:8 25=>7=>W B@><1>5<1>;VW ("). A:V;L:8 E2>@V, O:V ?@89<0NBL
0=B8?A8E>B8G=V 70A>18, G0AB> <0NBL =01CBV D0:B>@8 @878:C @>728B:C ", 4> B0 ?V4 G0A
;V:C20==O ?@5?0@0B< 3;>=V;® =5>1EV4=> 287=0G8B8 CAV ?>B5=FV9=V D0:B>@8 @878:C
@>728B:C " B0 268B8 ?>75@546C20;L=8E 70E>4V2 (482. @>74V; <>1VG=V @50:FVW)).
5 @5:><5=4CTBLAO ?@89<0B8 F59 ;V:0@AL:89 70AV1 >4=>G0A=> 7 0:;>3>;5<, ;52>4>?>N, 03>=VAB0
<8 4>?028E @5F5?B>@V2, ?@>B8?0@078B8G=8<8 70A>10<8, O:V <6CBL A?@8G8=8B8 ?0@>:A87
<0;L=C H;C=>G:>2C B0EV:0@4VN B8?C «?V@C5B» (torsades de pointes), 7 <5B04>=><<, V=H8<8
=59@>;5?B8:0<8 B0 ;V:0@AL:8<8 70A>10<8, O:V <6CBL A?@8G8=8B8 ?0@>:A87<0;L=C H;C=>G:>2C
B0EV:0@4VN B8?C «?V@C5B» (torsades de pointes), 482. @>74V; <>1VG=V @50:FVW)).
@07V 70AB>AC20==O ?@5?0@0BC =02VBL 2 =87L:8E 4>70E A;V4 72060B8 =0 @878: @>728B:C
?V7=L>W 48A:V=57VW, 7>:@5<0 A5@54 E2>@8E ;VB=L>3> 2V:C.
3;>=V;® <0T 0=B8E>;V=5@3VG=89 5D5:B, B>15@56=VABN A;V4 70AB>A>2C20B8 C ?0FVT=BV2 7
3;0C:>>N, :8H:>2>N =5?@>EV4=VABN, 2@>465=8< AB5=>7< (" , 70B@8N A5GV B0 3V?5@?;07VTN
?@>AB0B8 2 0=0<=57V.
3;>=V;® ?>B@V1=> 70AB>A>2C20B8 7 >15@56=VABNC ?0FVT=BV2 7V AE8;L=VABN 4>
3V?5@B5=7VW, >A>1;82> C ?0FVT=BV2 ;VB=L>3> 2V:C, G5@57 @878: 28=8:=5==O
3V?5@B>=VG=>3> :@87C.
&59 ;V:0@AL:89 70AV17C, B>3> 70AB>AC20B8 =5 @5:><5=4CTBLAO ?0FVT=B0< 7 =5?5@5=>A878,
;0:B07=>N =54>AB0B=VABN 01> A8=4@>>< =54>AB0B=>ABV 2A<>:BC20==O 3;N:>78 B0 30;0:B>78
(@V4:5 A?04:>25 70E2>@N20==O).

0AB>AC20==O C ?5@V>4 203VB=>ABV 01> 3>4C20==O 3@C44N.
03VB=VABL. # B20@8= A?>AB5@V30;>AO 7=865==O D5@B8;L=>ABV, ?>2070=5 7 D0@<0>;>3VG=8
<8 2;0AB82>ABO<8 ;V:0@AL:>3> 70A>1C (?@>;0:B8= >?>A5@54:>20=89 5D5:B). 57C;LB0B8
4>A;V465==O =0 B20@8=0E =5 2:07CNBL =0 157?>A5@54=V9 01> >?>A5@54:>20=89 H:V4;8289 ??;82
=0 ?5@51V3 203VB=>ABV, @>728B>: 5<1@V>=V2/?;>4V2 V/01> ?>AB=0B0;L=89 @>728B>.:)>4>
;N459 4>ABC?=0 4C65 >1<565=0 :V;L:VABL 40=8E ?@> ??;82 =0 ?5@51V3 203VB=>ABV. 0965 2 CAVE

28?04:0E ?>@CH5==O @>728B:C ?>4C 01> =>2>=0@>465=8E, ?@> O:V ?>2V4<>;O;>AO 2 :>=B5:ABV
70AB>AC20==O AC;L?V@84C ?V4 G0A 203VB=>ABV, 4>?CA:0NBLAO 0;LB5@=0B82=V ?>OA=5==O,
O:V 740NBLAO 1V;LH 2V@>3V4=8<8. "0:8< G8=><, G5@57 >1<565=89 4>A2V4 70AB>AC20==O
AC;L?V@84C ?V4 G0A 203VB=>ABV 9>3> 70AB>AC20==O =5 @5:>5=4CTBLAO. >2>=0@>465=V,
<0B5@V O:8E >B@8B8:8 (2.;NG0NG8 ?@5?0@0B 3;>=V;®) ?V4 G0A B@5BL>3> B@8<5AB@C
203VB=>ABV, ?VA;O =0@>465==O<0NBL @878: 28=8:=5==O =51060=8E 5D5:BV2, 2 B> A8
5@V>4 3>4C20==O 3@C44N. A:V;L:8 AC;L?V@8428O2;OTBLAO 2 3@C4=>

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.

!;V4 ?>?5@548B8 ?0FVT=BV2, >A>1;82> B8E, EB> :5@CT B@0=A?>@B=8<8 70A>10<8 G8 ?@0FNT 7
V=H8<8 <5E0=V7<0<8, ?@> B5, I> ?@89<0==O FL>3> ;V:0@AL:>3> 70A>1C <>65 ?@872>48B8 4>
@>728B:C A>=;82>ABV (482. @>74V; <>1VG=V @50:FVW»). V4 G0A 70AB>AC20==O ?@5?0@0BC
?@>B8?>:070=> :5@C20B8 02B>B@0=A?>@B< B0 ?@0FN20B8 7 V=H8<8 <5E0=V7<0<8.

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

;O ?5@>@0;L=>3> 70AB>AC20==O.

!;V4 702648 ?@87=0G0B8 □>@>A;V. >@>B:>B@820;5 A8<0B8G=5 ;V:C20==O B@82>6=8E AB0=V2 C
@07V, :>;8 728G09=V B5@0?52B8G=V 70E>48 =5 40;8 @57C;LB0BV2: 4>1>20 4>70 AB0=>28BL 50-150
<3 ?@>BO3><=5 1V;LH5 4 B86=V2.

VB8 2V:>< 2V4 6 @>:V2. !5@9>7=V ?>254V=:>2V @>7;048 (71C465==O, A0<>?>H:>465==O,
AB5@5>B8?VO) C 4VB59 2V:>< 2V4 6 @>:V2, >A>1;82> C ?0FVT=BV2 7 0CB8G=8<8 A8=4@><0<8: 5
<3/:3 <0A8 BV;0 =0 4>1C (70 =5>1EV4=>ABV FN 4>7C <>6=0 71V;LH8B8 4> 10 <3/:3 <0A8 BV;0 =0
4>1C).

VB8.

A:V;L:8 5D5:B82=VABL B0 157?5:0 70AB>AC20==O AC;L?V@84C 4VBG< 282G5=V =5 2 ?>2=>1AO7V,
9>3> A;V4 70AB>A>2C20B8 7 >15@56=VABN (482. @>74V; «!>AV1 70AB>AC20==O B0 4>78»). '5@57
2?;82, O:89 G8=8BL ?@5?0@0B =0 :>3=VB82=V 74V1=>ABV, @5:>5=4CTBLAO I>@VG=> ?@>2>48B8
;;V=VG=5 >1AB565==O 7 <5B>N >FV=:8 740B=>ABV 4> =02G0==O. 5>1EV4=> ?5@V>48G=>
>@83C20B8 4>7C ?@5?0@0BC, 28E>4OG8 7 ;;V=VG=>3> AB0BCAC 48B8=8.
0AB>AC20==O B25@48E :0?AC; 4VBO< 2V:>< 4> 6 @>:V2 ?@>B8?>:070=5, >A:V;L:8 F5 <>65
?@825AB8 4> >1BC@0FVW 48E0;L=8E H;OE2.

5@54>7C20==O.

>A2V4 I>4> ?5@54>7C20==O AC;L?V@84C >1<565=89. >6CBL A?>AB5@V30B8AO 48A:V=5B8G=V
?@>O28 7V A?07<0B8G=>N :@82>H8TN, ?@>B@C7VTN O78:0 B0 B@87<><. # 45O:8E E2>@8E
<>6CBL @>728=CB8AO ?@>O28 ?0@:V=A>=V7 O2;ONBL =5157?5:C 4;O 68BBO, 01> =02VBL :><0.
!C;L?V@84 G0AB:>2> 282>48BLAO ?@8 35<>4V0;V7V. !?5F8DVG=89 0=B84>B 4;O AC;L?V@84C
2V4ACB=V9.

V:C20==O<0T 1CB8 A8<0B8G=5, @50=V<0FVO ?@8 @5B5;L=>=B@>;V A5@F52>W 4VO;L=>ABV B0
48E0;L=>W DC=:FVW (@878: ?@>;>=30FVW V=B5@20;C QT B0 H;C=>G:>28E 0@8BB@V1=>
?@>4>26C20B8 4> ?>2=>3> >4C60==O E2>@>3>. # @07V @>728B:C BO6:>3> 5:AB@0?V@03> A8=4@>
48B8 0=B8E>;V=5@3VG=V ?@5?0@0B8.

>1VG=V @50:FVW.

51060=V @50:FVW, ?>2O70=V V7 70AB>AC20==O< ?@5?0@0BC, I> A?>AB5@V30;8AO ?V4 G0A
;;V=VG=8E 4>A;V465=L, =02>4OBLAO =86G5 70 ;;0A0<8 >@30=V2 B0 A8AB5< C ?>@O4:C 7
<5=H5==O G0AB>B8 28=8:=5==O.

52@>;>3VG=V @>7;048.

0==O 48A:V=57VO (A?0AB8G=0 :@82>H8O, >:C;>3V@=V :@878, B@87<), I> 7<5=HCTBLAO ?@8
70AB>AC20==V 0=B8E>;V=5@3VG=8E 0=B8?0@:V=A>=VG=8E ?@5?0@0BV2.

:AB@0?V@0

- ?0@:V=A>=V7< B0 A?>@V4=5=V A8<8: B@5<>@, 3V?5@B>=CA, 3V?>:V=57VO B0
3V?5@A0;V20FVO;
- 0:V=5B8G=V A8<8, I> AC?@>2>46CNBLAO 01> =5 AC?@>2>46CNBLAO 3V?5@:V=57<, O:V
G0AB:>2> 7<5=HCNBLAO ?@8 70AB>AC20==V 0=B8E>;V=5@3VG=8E 0=B8?0@:V=A>=VG=8E
035=BV2;
- 3V?5@:V=5B8G=0-3V?5@B>=VG=0, 71C4;820 @CE>20 0:B82=VABL;
- 0:0B87VO.
V7=O 48A:V=57VO, 4;O O:>W E0@0:B5@=V <8<>2V;L=V @8B:@5<0 O78:0 V/01> >1;8GGO, B0 O:0
<>65 A?>AB5@V30B8AL C E>4V B@820;8E :C@AV2 ;V:C20==O 2AV<0 =59@>;5?B8:0<8; 2 FL>
;V=5@3VG=V 0=B8?0@:V=A>=VG=V ?@5?0@0B8 =55D5:B82=V B0 <>6CBL ?>3V@HC20B8 ;V=VG=V
?@>O28.
0A?>:V9;8289 5D5:B 01> A>=:82VABL.
04E>48;8 ?>2V4<>;5==O ?@> 157A>==O B0 715=B565=VABL.
!C4><8 (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

>B5=V9=> ;5B0;L=89 7;>O:VA=89 =59@>;5?B8G=89 A8=4@< (482. @>74V; «A>1;82>ABV
70AB>AC20==O»).

030;L=V @>7;048.
1V;LH5==O <0A8 BV;0.
>@CH5==O VW A8AB5<8.
=0DV;0:B8G=V @50:FVW, 7048H:0 B0 0=0DV;0:B8G=89 H>:.
=4>:@8==V ?>@CH5==O.
>@>B:>G0A=0 3V?5@?@>;0:B8=5 7=8:0T ?VA;O 2V4ABV, 71V;LH5==O <>;>G=8E 70;>7 B0 1>;V C
<>;>G=8E 70;>70E.
0@4V>;>3VG=V @>7;048.
>4>265==O QT-V=B5@20;C, H;C=>G:>2V 0@8B:@5<0 ?0@>:A87<0;L=0 H;C=>G:>20 B0EV:0@4VO
B8?C «?V@C5B» (torsades de pointes) B0 H;C=>G:>20 B0EV:0@4VO, O:0 <>65 ?@8725AB8 4>
DV1@8;OFVW H;C=>G:V2 01> 7C?8=:8 A5@FO, @0?B>20 A<5@BL (482. @>74V; «A>1;82>ABV
70AB>AC20==O»).

!C48==V ?>@CH5==O.
@B>AB0B8G=0 0@B5@V0;L=0 3V?>B5=7VO, ?V428I5==O 0@B5@V0;L=>3> B8A:C.
>ABC@0;L=0 3V?>B5=7VO.
V4 G0A 70AB>AC20==O 0=B8?A8E>B8G=8E 70A>1V2 ?>2V4<>;O;>AL ?@> 28?04:8 25=>7=>W B@>
<1>5<1>;VW, 2;;NG0NG8 V=>4V ;5B0;L=V 28?04:8 5<1>;VW ;535=52>W 0@B5@VW B0 B@<1>7
3;81>:8E 25= G0AB>B0 28?04:V2 =5 2AB0=>2;5=0.
I>:C A8AB5<8 :@>2V B0 ;VW A8AB5<8.
59:>?5=VO, =59B@>?5=VO B0 03@0=C;>F8B>7 G0AB>B0 28=8:=5==O =52V4><0.
I>:C 35?0B>1V;V0@=>W A8AB5<8.
1V;LH5==O 0:B82=>ABV D5@<5=BV2 ?5GV=:8.
0B>;>3VO H:V@8 B0 ?V4H:V@=>W B:0=8=8.
0:C;>?0?C;O@=89 28A8?, :@>?82O=:0.
030;L=V @>7;048.
50:FVW 3V?5@GCB;82>ABV.
!B0=8 ?@8 203VB=>ABV, 2 ?VA;O?>;>3>2>4V.
18=4@<> 2V42=>0@>465=8E G0AB>B0 28=8:=5==O =52V4><0.

"5@ABV.
3 @>:8.

#<>28 715@V30==O. □15@V30B8 2 =54>ABC?=>@83V=0;L=V9 C?0:>2FV ?@8 B5□.

#?0:>2:0.

30 (15E2): ?> 15 :0?AC; C 1;VAB5@V; ?> 2 1;VAB5@8 C :0@B>==V9 :>@>1FV.
30 (30E1): ?> 30 :0?AC; C 1;VAB5@V; ?> 1 1;VAB5@C C :0@B>==V9 :>@>1FV.

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

8@>1=8.. !0=>DV V=B@>? =40AB@V0.

**VAF57=0E>465==O 28@>1=8:0 B0 9>3> 04@5A020465==O 4VO;L=>ABV.6, 1C;L20@ 45 ;.@>?, 21800
25B83=8, \$@0=FVO.**