

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

§, 75
(FLAMOGREL 75)

!::04:

4VNG0 @5G>28=0: clopidogrel;
1 B01;5B:0, 2:@8B0 ?;V2:>2>N >1>;>=:>N, ?V4>3@5;C 1VAC;LD0BC 2 ?5@5@0EC20==V =0
;>?V4>3@5; 75 <3;
4>?>28=8: F5;N;>70 :@8AB0;VG=0, ;0:B>70, <=>3V4@0B, =0B@VN :@>A:0@<5;>70,
3V4@>:A8?@>?V;F5;N;>70 =87L:>70A?8@B V7>?@>?V;>289, 48E;>@<5B0=.

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. □=B8B@><1>B8G=V 70A>18. >4 " ! B01A C04.

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

>:070==O.

@>DV;0:B8:0 ?@>O2V2 0B5@>B@><1>7C C 4>@>A:8E:

□ C E2>@8E, O:V ?5@5=5A;8 V=D0@:B :0@40 (?>G0B>: ;V:C20==O - G5@57 :V;L:0 4=V2, 0;5 =5
?V7=VH5 =V6 G5@57 35 4=V2 ?VA;O 28=8:=5==O), VH5G0B>: ;V:C20==O - G5@57 7 4=V2, 0;5 =5
?V7=VH5 =V6 G5@57 6 C O:8E 4V03=>AB>20=> 70E2>@N20==O ?5@8D5@8G=8E 0@B5@V9
(C@065==O 0@B5@V9 V 0B5@>B@><1>7 AC48= =86=VE :V=FV2>);

□ C E2>@8E V7 3>AB@8< :>@>=0@=8< A8=4@>><

V7 3>AB@8< :>@>=0@=8< A8=4@>>< 157 ?V49>:0@40 157 7C1FO Q), C B>

V7 3>AB@8< V=D0@:B>< :0@40 7 ?V49>><< A53<5=B0 ST C :><1V=0FVW 7 !(C E2>@8E, O:V >B@8
@>DV;0:B8:0 0B5@>B@><1>B8G=8E B0 B@><1>5<1>;VG=8E ?>4V9 ?@8 DV1@8;OFVW
?5@54A5@4L

;>?V4>3@5; C :><1V=0FVW 7 !?>:070=89 4>@>A;8< ?0FVT=B0< 7 DV1@8;OFVTN ?5@54A5@4L, O:V
<0NBL I>=09<5=H5 >48= D0:B>@ @878:C 28=8:=5==O AC48==8E ?>4V9, C O:8E VA=CNBL
?@>B8?>:070==O 4> ;V:C20==O 0=B03>=VAB0<8 2VB0
;O >B@8<0==O 4>40B:>2>W V=D@>@<0FVW 482. @>74V; «\$0@<0:>;>3VG=V 2;0AB82>ABV».

@>B8?>:070==O.

V428I5=0 GCB;82VABL 4> 4VNG>W @5G>28=8 01> 4> 1C4L-O:>3> :>5=B0 ?@5?0@0BC. "O6:0
?5GV=:>20 =54>AB0B=VABL. >AB@0 :@>2>B5G0 (=0?@8::04, ?5?B8G=0 28@07:0 01>
2=CB@VH=L>G5@5?=89 :@>2>28;82).

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

>@>A;V B0 E2>@V ;VB=L>3> 2V:C. \$;0<>3@5;L 75 ?@87=0G0NBL ?> 75 <3 >48= @07 =0 4>1C,
=570;56=> 2V4 ?@89>

E2>@8E V7 3>AB@8< :>@>=0@=8< A8=4@>>< 157 ?V49> (=5AB01V;L=0 AB5=>:0@4VO 01>
V=D0@:B :0@40 157 7C1FO Q =0) ;V:C20==O ;;>?V4>3@5;5< ?>G8=0NBL 7 >4=>@07>2>W
=020=B06C20;L=>W 4>78 300 <3, 0 ?>BV< ?@>4>26CNBL 4>7>N 75 <3 >48= @07 =0 4>1C (7 !C 4>7V
75325 <3 =0 4>1C). A:V;L:8 70AB>AC20==O 1V;LH 28A>:8E 4>7 !?V428ICT @878: :@>2>B5GV, @5:>
<5=4CTBLAO =5 ?5@528IC20B8 4>7C !100 <3. ?B8<0;L=0 B@820;VABL ;V:C20==O D>@<0;L=> =5
2AB0=>2;5=0. 57C;LB0B8 ;;V=VG=8E 4>A;V465=L A2V4G0BL =0 :>@8ABL 70AB>AC20==O
?@5?0@0BC 4> 12

E2>@8E V7 3>AB@8< V=D0@:B>< :0@40 7 ?V49>><< A53<5=B0 ST ;;>?V4>3@5; ?@87=0G0NBL
?>
75 <3 >48= @07 =0 4>1C, ?>G8=0NG8 7 >4=>@07>2>W =020=B06C20;L=>W 4>78 300 <3 C :><1V=0FVW
7 !, 7 70AB>AC20==O< B@><1>;VB8G=8E ?@5?0@0BV2 01> 157 =8E. V:C20==O E2>@8E AB0@H5 75
@>:V2 ?>G8=0NBL 157 =020=B06C20;L=>W 4>78 ;;>?V4>3@5;C. ><1V=>20=C B5@0?VN A;V4
?>G8=0B8 O:>>30 @0=VH5 ?VA;O ?>O28 A8>26C20B8 ?@8=09<=V G>B8@8 B86=V. >@8ABL 2V4 :>
<1V=0FVW ;;>?V4>3@5;C 7 !?>=04 G>B8@8 B86=V ?@8 FL>@N20==V =5 282G0;0AO.

?0FVT=BV2 7 DV1@8;OFVTN ?5@54A5@4L ;;>?V4>3@5; 70AB>A>2CNBL C >4=>:@0B=V9
4>1>2V9 4>7V
75 <3. 07>< V7 ;;>?V4>3@5;5< A;V4 @>7?>G0B8 B0 ?@>4>26C20B8 70AB>AC20==O !(C 4>7V 75-100
<3 =0 4>1C) (482. @>74V; «\$0@<0:>;>3VG=V 2;0AB82>ABV»).

28?04:C ?@>?CA:C 4>78:
- O:I> 7 <><5=BC, ;>;8 ?>B@V1=> 1C;> ?@89<0B8 G5@3>2C 4>7C <8=C;> <5=H5 12 3>48=: ?0FVT=B
<0T =5309=> ?@89=OB8 ?@>?CI5=> 4>7C, 0 =0ABC?=C 4>7C 265 ?@89<0B8 C 728G=89 G0A.
- O:I> <8=C;> 1V;LH5 12 3>48=, ?0FVT=B <0T ?@89<0B8 =0ABC?=C G5@3>2C 4>7C C 728G09=89 G0A
B0 =5 ?>42>N20B8 4>7C 7 <5B>N :>?CI5=>W 4>78.
VB8 B0 ?V4;VB:8. ;>?V4>3@5; =5 A;V4 70AB>A>2C20B8 4VBO<, >A:V;L:8 =5<0T 40=8E I>4>
5D5:B82=>ABV ?@5?0@0BC (482. @>74V; «\$0@<0:>48=0
8@:>20 =54>AB0B=VABL. "5@0?52B8G=89 4>A2V4 70AB>AC20==O ?@5?0@0BC ?0FVT=B0< 7
=8@:>2>N =54>AB0B=VABN >1<565=89 (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

5GV=:>20 =54>AB0B=VABL. "5@0?52B8G=89 4>A2V4 70AB>AC20==O ?@5?0@0BC ?0FVT=B0< V7
70E2>@N20==O<8 ?5GV=:8 A5@54=L>W BO6:>ABV B0 <>6;82VABN 28=8:=5==O 35<>@03VG=>3>
4V0B57C >1<565=89 (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

>1VG=V @50:FVW.

>1VG=V @50:FVW @>7?>4V;5=V 70 A8AB5<N >@30=V2, G0AB>B0 WE 28=8:=5==O 287=0G5=0 B0:8
< G8=>H8@5=V (2V4 □ 1/100 4> □1/10), =5?>H8@5=V (2V4 □ 1/1000 4> □1/100), @V4:> ?>H8@5=V (2V4
□ 1/10000 4> □1/1000), 4C65 @V4:> ?>H8@5=V (< 1/10000), G0AB>B0 =52V4<0. ;O :>6=>3> ;:0AC
A8AB5<8 >@30=V2 ?>1VG=V 5D5:B8 707=0G5=V C ?>@O4:C 7=865==O WE BO6:>ABV.

!8AB5<8 >@30=V2	>H8@5=V	5?>H8@5=V	V4:> ?>H8@5=V	C65 @V4:> ?>H8@5=V, G0AB>B0 =52V4<0*
@>2 B0 ;V		"@> <1>F8B>?5=VO, 59:>F8B>?5=VO, 5>78=>DV;VO	59B@>?5=VO, 2;;NG0NG8 BO6:C =59B@>?5=VN	"@><1>B8G=0 B@> <1>F8B>?5=VG=0 ?C@?C@0 ("") (482. @>74V; «A>1;82>ABV 70AB>AC20==O»), 0?;0AB8G=0 0=5?5=VO, 03@0=C;>F8B>7, BO6:0 B@><1>F8B>?5=VO, =01CB0 35<>DV;VO , 3@0=C;>F8B>?5=VO, 0=5
				!8@>20B:>20 E2>@>10, 0=0DV;0:B>W4=V @50:FVW, ?5@5E@5AB=0 3V?5@GCB;82VABL ?> ?V@848=V2 (B0:8E O: B8;>?V48=, ?@0AC3@5;L) (482. @>74V; «A>1;82>ABV 70AB>AC20==O»)
A8EV0B@8G=V ?>@CH5==O				0;NF8=0FVW, A?;CB0=VABL A2V4> <>ABV

!8AB5<8 >@30=V2	>H8@5=V	5?>H8@5=V	V4:> ?>H8@5=V	C65 @V4:> ?>H8@5=V, G0AB>B0 =52V4><0*
5@2>20 A8AB5 <0 @30=8 7>@C		=CB@VH=L>- G5@5?=V :@>2>B5GV (C 45O:8E 28?04:0E 7 ;5B0;L=8< =0A;V4:><), 3>;>2=89 1V;L, ?0@5AB57VO, 70?0<>@>G5==O @>2>B5G0 2 4V;O=:C >:0 (:>=N=:B820;L=0, >:C;O@=0, @5B8=0;L=0)		
@30=8 A;CEC B0 ;01V@8=BC			0?0 <>@>G5==O	
!C48==0 A8AB5 <0	5<0B><0			"O6:89 :@>2>28;82, :@>2>B5G0 7 >?5@0FV9=>W @0=8, 20A:C;VB, 0@B5@V0;L=0 3V?>B5=7VO
5A?V@0B>@=V, B>@0:0;L=V B0 <54V0AB8- =0;L=V ?>@CH5==O	>A>20 :@>2>B5G0			@>2>B5GV @5A?V@0B>@=>3> H;OEC (:@>2>E0@:0==O, ;535=52V :@>2>B5GV), 1@>=E>A?07<, V=B5@AB8FV0;L=89 ?=52<>=VB, 5>78=>DV;L=0 ?=52 <>=VO
(;C=:>2>- :8H:>289 B@0:B	(;C=:>2>- :8H:>2V :@>2>B5GV, 4V0@5O, 014>	8@07:0 H;C=:0 B0 420=04FOB8?0- ;>W :8H:8, 30AB@8B, 1;N20==O, =C4>B0, 70?>@, <5B5>@87<	5B@>?5@8- B>=50;L=89 :@>2>28;82	(;C=:>2>-:8H:>2V B0 @5B@>?5@8B>=50;L=V :@>2>B5GV 7 ;5B0;L=8 <=0A;V4:><, ?0=:@50B8B, :>;VB (7>:@5<0 28@07:>289 01> ;VF8B0@=89), AB> <0B8B
5?0B>1V;V- 0@=0 A8AB5<0				>AB@0 ?5GV=:>20 =54>AB0B=VABL, 35?0B8B, 0=><0;L=V @57C;LB0B8 ?>:07=8:V2 DC=:FVW ?5GV=:8
(:V@0 B0 ?V4H:V@=0 ;VB:>28=0	V4H:V@- =89 :@>2>28;82	8A8?0==O, A25@1V6, 2=CB@VH=L>- H:V@=V :@>2>28;828 (?C@?C@0)		C;L>7=89 45@<0B8B (B>:A8G=89 5?V45@ <0;L=89 =5:@>;V7, A8=4@>< !BV25=A0- 6>=A>=0, @<=0 5@8B5 <0), 0=3V>=52@>B8G=89 =01@O:, 5@8B5

!8AB5<8 >@30=V2	>H8@5=V	5?>H8@5=V	V4:> ?>H8@5=V	C65 @V4:> ?>H8@5=V, G0AB>B0 =52V4><0*
VAB:>2>- <'O7:>20 A8AB5 <0, A?>;CG=0 B0 :VAB:>20 B:0=8=8				<0B>7=5 28A8?0==O, :@>?82O=:0, <548:0 <5=B>7=89 A8=4@<< 3V?5@GCB;82>ABV, <548:0<5=B>7=0 28A8?:0 7 5>78=>DV;VTN B0 A8AB5<=8<8 ?@>O20<8 (DRESS A8=4@<<), 5:75 <0, ?;5A:0B89 ;8H09 VAB:>2>-<O7:>2V :@>2>28;828 (35 <0@B@>7), 0@B@8B, 0@B@0;3VO,
8@:8 B0 A5G>284V;L-=0 A8AB5<0		5<0BC@VO		;<5@C;>=5D@8B, ?V428I5==O @V2=O :@50B8=V=C 2 :@>2V
030;L=89 AB0= V @50:FVW C	@>2>B5GV C			0@OG:0
01>@0B>@=V 4>A;V465==O		>4>265==O G0AC :@>2>B5GV, 7=865==O		
		:V;L:>ABV =59B@>DV;V2 V B@><1>F8BV2		

* =D>@<0FVO AB>A>2=> ::>?V4>3@5;N 7 G0AB>B>N «G0AB>B0 =52V4><0».

5@54>7C20==O.

@8 ?5@54>7C20==V ::>?V4>3@5;C <65 A?>AB5@V30B8AO ?>4>265==O G0AC :@>2>B5GV 7
=0ABC?>8<8 CA:;04=5==O<8. # @07V 28=8:=5==O :@>2>B5GV @5:>5=4CTBLAO A8<0B8G=5
;V:C20==O.
=B84>B D0@<0:>;>3VG=>W 0:B82=>ABV ::>?V4>3@5;C =5 2V4><89. @8 =5>1EV4=>ABV =5309=>3>
:>@83C20==O ?>4>265=>3> G0AC :@>2>B5GV 4VO ::>?V4>3@5;C <65 1CB8 ?@8?8=5=0 ?5@5;820==O
< B@><1>F8B0@=>W <0A8.

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

'5@57 2V4ACB=VABL ;;V=VG=8E 40=8E I>4> 70AB>AC20==O ::>?V4>3@5;C C ?5@V>4 203VB=>ABV
=51060=> ?@87=0G0B8 ?@5?0@0B 203VB=8< 6V=:0< (70AB5@56=89 70EV4).
>A;V48 =0 B20@8=0E =5 28O28;8 ?@O<>3> 01> >?>A5@54:>20=>3> =530B82=>3> ?;82C ::>?V4>3@5;C
=0 203VB=VABL, @>728B>: 5<1@V>=0/?;>40, ?>;>38 B0 ?>AB=0B0;L=89 @>728B>:.
5 2V4><>, G8 5:A:@5BCTBLAO ::>?V4>3@5;C 3@C4=5 <>;>: . # 4>A;V465==OE =0 B20@8=0E 1C;>
?>:070=>, I> ::>?V4>3@5;C 5:A:@5BCTBLAO 2 3@C4=5 <>;>:, B> ;V:C20==O ?@5?0@0B< \$;0
<>3@5;L 75 3>4C20==O 3@C44N A;V4 ?@8?8=8B8.
\$5@B8;L=VABL. V4 G0A 4>A;V465=L =0 ;01>@0B>@=8E B20@8=0E =5 1C;> 28O2;5=> =530B82=>3>
?;82C ::>?V4>3@5;C =0 D5@B8;L=VABL.

VB8.

::>?V4>3@5; =5 A;V4 70AB>A>2C20B8 4VBO<, >A;V;L:8 =5<0T 40=8E I>4> 5D5:B82=>ABV ?@5?0@0BC
(482. @>74V; «\$0@<0:>48=0

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

@>2>B5G0 B0 35<0B>;>3VG=V @>7;048.
'5@57 @878: @>728B:C :@>2>B5GV B0 35<0B>;>3VG=8E ?>1VG=8E 4V9 A;V4 =5309=> ?@>25AB8

@>73>@=CB89 0=0;V7 :@>2V B0/01> V=HV 2V4?>2V4=V B5AB8, O:I> ?V4 G0A 70AB>AC20==O
?@5?0@0BC A?>AB5@V30NBLAO A8<8, I> A2V4G0BL ?@> <>6;82VABL :@>2>B5GV (482. @>74V;
«>1VG=V @50:FVW»). /: V V=HV 0=B8B@<1>F8B0@=V 70A>18, ;:>?V4>3@5; A;V4 >15@56=>
70AB>A>2C20B8 ?0FVT=B0< 7 ?V428I5=8< @878:< :@>2>B5GV 2=0A;V4>: B@02<8,
EV@C@3VG=>3> 2B@CG0==O 01> V=H8E ?0B>;>3VG=8E AB0=V2, 0 B0:>6 C @07V 70AB>AC20==O
?0FVT=B0<8 !, 35?0@8=C, V=3V1VB>@V2 3;V:>?@>B5W=C IIB/III 01> =5AB5@>W4=8E
?@>B870?0;L=8E ?@5?0@0BV2, 7>:@5<0 V=3V1VB>@V2 &-2. 5>1EV4=> C206=> AB568B8 70 ?@>O20
<8 C E2>@8E A82>B5GV, C B>20=>W :@>2>B5GV, >A>1;82> C ?5@HV B86=V ;V:C20==O B0/01>
?VA;O V=207V9=8E ?@>F54C@ =0 A5@FV B0 EV@C@3VG=8E 2B@CG0=L. 4=>G0A=5
70AB>AC20==O ;:>?V4>3@5;C 7 ?5@>@0;L=8<8 0=B8:>03C;O=B0<8 =5 @5:<5=4CTBLAO, >A:V;L:8
2V= <>65 ?>A8;8B8 V=B5=A82=VABL :@>2>B5G (482. @>74V; «70T<>4VO 7 V=H8<8 ;V:0@AL:8<8
70A>10<8 B0 V=HV 2848 270T<>4V9»).

28?04:C ?;0=>2>3> EV@C@3VG=>3> 2B@CG0==O, I> B82> =5 ?>B@51CT 70AB>AC20==O 0=B8B@>
<1>F8B0@=8E 70A>1V2, ;V:C20==O ;:>?V4>3@5;5< A;V4 ?@8?8=8B8 70 7 4=V2 4> >?5@0FVW.
0FVT=B8 ?>28==V ?>2V4<;OB8 ;V:0@O<, 2 B> AB<<0B>;>30<, ?@> B5, I> 2>=8 ?@89<0NBL
;:>?V4>3@5;, ?5@54 ?@87=0G5==O <W <1C4L-O:>W >?5@0FVW G8 ?5@54 70AB>AC20==O< =>2>3>
;V:0@AL:>3> 70A>1C. ;>?V4>3@5; ?>4>26CT B@820;VABL :@>2>B5GV, B3> A;V4 >15@56=>
70AB>A>2C20B8 ?0FVT=B0< 7 ?V428I5=8< @878:< :@>2>B5GV (>A>1;82> H;C=:>2>-.8H:>2>W 9
2=CB@VH=L>>G=>W).

0FVT=BV2 A;V4 ?>?5@548B8, I> ?V4 G0A ;V:C20==O ;:>?V4>3@5;5< (:@5<> 01> C :<<1V=0FVW 7 !)
:@>2>B5G0 <>65 7C?8=OB8AO ?V7=VH5, =V6 728G09=>, V I> 2>=8 ?>28==V ?>2V4<;OB8 ;V:0@O
?@> :>6=89 28?04>: =5728G=>W (70

"@><1>B8G=0 B@><1>F8B>?5=VG=0 ?C@?C@0 ("").

C65 @V4:> A?>AB5@V30;8AO 28?04:8 ""?VA;O 70AB>AC20==O ;:>?V4>3@5;C, V=>4V =02VBL ?VA;O
9>3> :>@>B:>G0A=>3> 70AB>AC20==O. ""?@>O2;OTBLAO B@><1>F8B>?5=VTN B0
0=3V>?0B8G=>N 35<;VB8G=>N 0=5;>3VG=8<8 ?@>O20<8, 48ADC=:FVTN =8@>: 01> 30@OG:>N. ""T
?>B5=FV9=> AB0=<< I> 703@>6CT 68BBN B0 ?>B@51CT =5309=>3> ;V:C20==O, 7>:@5<0 ?;07

<>D>@57>

01CB0 35<>DV;VO.>2V4<<O;>AO ?@> 28?04:8 @>728B:C =01CB>W 35<>DV;VW ?VA;O
70AB>AC20==O ;:>?V4>3@5;C. # 28?04:0E ?V4B25@465=>3> V7>;L>20=>3> 71V;LH5==O ""
(0:B82>20=>3> G0AB:>2>3> B@><1>?;0AB8=>2>3> G0AC), I> AC?@>2>46CTBLAO 01> =5
AC?@>2>46CTBLAO :@>2>B5G5N, ?8B0==O ?@> 4V03=>ABC20==O =01CB>W 35<>DV;VW ?>28==>
1CB8 @>73;O=CB>. 0FVT=B8, 7 ?V4B25@465=8< 4V03=>7><< =01CB>W 35<>DV;VW ?>28==V
7=0E>48B8AO ?V4 =03;O4<< ;V:0@O V >B@8AC20==O ;:>?V4>3@5;C ?>28==> 1CB8 ?@8?8=5=>.
5I>402=> ?5@5=5A5=89 VH5

'5@57 =54>AB0B=VABL 40=8E =5 @5:<5=4CTBLAO ?@87=0G0B8 ;:>?V4>3@5; C ?5@HV 7 4=V2
?VA;O 3>AB@>3> VH53> V=AC;LBC.

&8B>E@>< 450 2 !19 (CYP2C19).

\$0@<0:>35=5B8:0: # ?0FVT=BV2 V7 35=5B8G=> 7=865=>N DC=:FVTN CYP2C19 A?>AB5@V30TBLAO
<5=H0 :>=F5=B@0FVO 0:B82=>3> <5B01>;VBC ;:>?V4>3@5;C C ?;07:0@40 ?>@V2=O=> 7 ?0FVT=B0<8
V7 =>@<0;L=8< DC=:FV=>C20==O< CYP2C19. 0@07 VA=CNBL B5AB8, O:V 40NBL 7>3C 28O28B8
35=>B8? CYP2C19 C ?0FVT=B0.

A:V;L:8 ;:>?V4>3@5; ?5@5B2>@NTBLAO C A2V9 0:B82=89<5B01>;VB G0AB:>2> ?V4 4VTN CYP2C19,
B> 70AB>AC20==O ?@5?0@0BV2, O:V 7=86CNBL 0:B82=VABL FL>3> D5@<5=BC, =09V<>2V@=VH5,
?@872545 4> 7<5=H5==O :>=F5=B@0FVW 0:B82=>3> <5B01>;VBC ;:>?V4>3@5;C C ?;071V6=89 70EV4
c;V4 C=8:0B8 >4=>G0A=>3> 70AB>AC20==O ?@5?0@0BV2, O:V ?@83=VGCNBL 0:B82=VABL
CYP2C19 (482. @>74V; «70T<>4VO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9»;
?5@5;V: V=3V1VB>@V2 CYP2C19 =02545=> C @>74V;V «\$0@<0:>:V=5B8:0»).

5@5E@5A=0 @50:B82=VABL ?>?V@848=V2. 0FVT=BV2 A;V4 ?5@52V@8B8 I>4> =0O2=>ABV 2 0=0
<=57V 3V?5@GCB;82>ABV 4> V=H8E BVT=>?V@848=V2 (B0:8E O: B8;:>?V48=, ?@0AC3@5;L), B>
=04E>48;8 ?>2V4<<5==O ?@> ?5@5E@5AB=C @50:B82=VABL ?>?V@848=V2 (482. @>74V; «>1VG=V
@50:FVW»). 0AB>AC20==O BVT=>?V@848=V2 <>65 ?@8725AB8 4> 28=8:=5==O 2V4 ;53:8E 4> 206:8E
0;5@3VG=8E @50:FV9, B0:8E O: 28A8?, =01@O: 2V=:5, 01> 35<0B>;>3VG=8E @50:FV9, B0:8E O: B@>
<1>F8B>?5=VO V =59B@>?5=VO. 0FVT=B8, O:V 2 <8=C;>

>@CH5==O DC=:FVW =8@>.:
"5@0?52B8G=89 4>A2V4 70AB>AC20==O :;>?V4>3@5;C ?0FVT=B0< 7 =8@:>2>N =54>AB0B=VABN >1
<565=89, B>
>@CH5==O DC=:FVW ?5GV=:8.
>A2V4 70AB>AC20==O ?@5?0@0BC ?0FVT=B0< V7 70E2>@N20==O<8 ?5GV=:8 A5@54=L>W
B06:>ABV B0 <>6;82VABN 28=8=:5==O 35<>@03VG=>3> 4V0B57C >1<565=89. ">
>?>28=8.

\$.0<>3@5;L 75 7C. ">78, 45DVF8B ;0:B078 0??0 01> ?>@CH5==O <0;L01A>@1FVW 3;N:>78-30;0:B>78,
=5 ?>28==V ?@89<0B8 F59 ?@5?0@0B.
\$.0<>3@5;L 75 ;VN @8F8=>2C 3V4@>35=V7>20=C, O:0 <>65 A?@8G8=OB8 @>7;04 H;C=:0 B0 4V0@5N.
/:I> ?0FVT=B 701C2 ?@89=OB8 4>7C ?@5?0@0BC, V <8=C;> <5=H5 12 3>48= ?VA;O ?;0=>2>3> ?@89>
?@5?0@0B =5>1EV4=> ?@89=OB8 O:=09H284H5, ?VA;O G>3> =0ABC?=C 4>7C A;V4 ?@89=OB8
2G0A=>. /:I> <8=C;> 1V;LH5 12 3>48= A;V4 ?@>?CAB8B8 ?@89> 701CB>W 4>78 V ?@89=OB8 2G0A=>
=0ABC?=C 4>7C ?@5?0@0BC. 54>?CAB8<> ?@89<0B8 ?>42V9=C 4>7C ?@5?0@0BC.
V4 G0A ;V:C20==O ?@5?0@0B<=5 A;V4 26820B8 0;:>3>;L G5@57 ?V428I5==O @878:C H;C=:>2>-
:8H:>2>W :@>2>B5GV.

A>1;82V 70AB5@565==O I>4> 2840;5==O 70;8H:V2 B0 2V4E>4V2
C4L-O:89 =528:>@8AB0=89 ?@5?0@0B 01> 2V4E>48 ?>B@V1=> 7=8I8B8 2V4?>2V4=> 4>

**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.**

;:>?V4>3@5; =5 2?;820T 01><0T =57=0G=89 2?;82 =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.

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

5@>@0;L=V 0=B8:>03C;O=B8. 4=>G0A=5 70AB>AC20==O ?@5?0@0BC \$.0<>3@5;L 75 7 >@0;L=8<8
0=B8:>03C;O=B0<8 =5 @5:><5=4CTBLAO, >A:V;L:8 B0:0 :<1V=0FVO <>65 ?>A8;8B8
V=B5=A82=VABL :@>2>B5GV (482. @>74V; «A>1;82>ABV 70AB>AC20==O»). %>G0 70AB>AC20==O
;>?V4>3@5;C C 4>7V 75 <3 =0 4>1C =5 74=5 =>@<0;V7>20=5 A?V22V4=>H5==O (!) C ?0FVT=V2, O:V
2?@>4>26 B@820;>3> G0AC >B@8<, >4=>G0A=5 70AB>AC20==O :;>?V4>3@5;C B0 20@D0@8=C
71V;LHCT @878: :@>2>B5GV G5@57 VA=C20==O =570;56=>3> 2?;82C =0 35>AB07.
=3V1VB>@8 3;V:>?@>B5W=C b/III0. ;:>?V4>3@5; A;V4 7 >15@56=VABN ?@87=0G0B8 ?0FVT=B0< V7
?V428I5=8< @878:< :@>2>B5GV G5@57 B@02 V=HV ?0B>;>3VG=V AB0=8, ?@8 O:8E >4=>G0A=>
70AB>A>2CNBL V=3V1VB>@8 3;V:>?@>B5W=C b/III0 (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).
F5B8;A0;VF8;>20 :8A;>B0 (!). F5B8;A0;VF8;>20 :8A;>B0 =5 7@=C 4VN :;>?V4>3@5;C =0 \$-V=4C:>20=C
03@530FVN B@><1>F8BV2, 0;5 :;>?V4>3@5; ?>A8;NT 4VN !=0 03@530FVN B@><1>F8BV2,
V=4C:>20=C :;>035=>B5 >4=>G0A=5 70AB>AC20==O 500 <3 !420 @078 =0 4>1C ?@>B03<< >4=>3>
4=O =5 A?@8G8=N20;> 7=0GCI>3> 71V;LH5==O G0AC :@>2>B5GV, ?>4>265=>3> 2=0A;V4>: ?@89>
?V4>3@5;C. A:V;L:8 <>6;820 D0@<0:>48=0?V4>3@5;5< V !7 ?V428I5==O< @878:C :@>2>B5GV,
>4=>G0A=5 70AB>AC20==O F8E ?@5?0@0BV2 ?>B@51CT >15@56=>ABV (482. @>74V; «A>1;82>ABV
70AB>AC20==O»).

5?0@8=. 0 40=8<8 :;V=VG=>3> 4>A;V465==O, ?@>2545=>3> =0 74>@>28E 4>1@>2>;LFOE,
;>?V4>3@5; =5 ?>B@51C202 :>@83C20==O 4>78 35?0@8=C B0 =5 703C;OFVN. 4=>G0A=5
70AB>AC20==O 35?0@8=C =5 7 V=3V1CNGC 4VN :;>?V4>3@5;C =0 03@530FVN B@><1>F8BV2.
A:V;L:8 <>6;820 D0@<0:>48=0?V4>3@5;5< V 35?0@8=< V7 ?V428I5==O< @878:C :@>2>B5GV,
>4=>G0A=5 70AB>AC20==O F8E ?@5?0@0BV2 ?>B@51CT >15@56=>ABV.
"@><1>;VB8G=V 70A>18. 57?5:0 >4=>G0A=>3> 70AB>AC20==O :;>?V4>3@5;C,
DV1@8=>A?5F8DVG=8E 01> DV1@8=>=5A?5F8DVG=8E B@><1>;VB8G=8E 035=V2 B0 35?0@8=C
1C;0 4>A;V465=0 C E2>@8E V7 3>AB@8< V=D0@:B< :0@40. '0AB>B0 :;V=VG=> 7=0GCI>W
:@>2>B5GV 1C;0 0=0;>3VG=>N BV9, I> A?>AB5@V30;0AO ?@8 >4=>G0A=>AC20==V B@>
<1>;VB8G=8E ?@5?0@0BV2 B0 35?0@8=C 7!(482. @>74V; «>1VG=V @50:FVW»).

5AB5@>W4=V ?@>B870?0;L=V ?@5?0@0B8 (). # :;V=VG=>A;V465==V, ?@>2545=>@>28E
4>1@>2>;LFOE, >4=>G0A=5 70AB>AC20==O :;>?V4>3@5;C B0 =0?@>:A5=C 71V;LHC20;> :V;L:VABL
?@8E>20=8E H;C=:>2>-.8H:>28E :@>2>B5G. 4=0: G5@57 2V4ACB=VABL 4>A;V465=L I>4> 270T

<>4VW ?@5?0@0BC 7 V=H8<8 4>B5?5@ =5 7OA>20=>, G8 7@>AB0T @878: H;C=:>2>:-:8H:>28E
:@>2>B5G ?@8 70AB>AC20==V 7 CAV<0 . ">1EV4=0 >15@56=VABL ?@8 >4=>G0A=>AC20==V , 7>:@5
<0 V=3V1VB>@V2 &-2, 7 ;:>?V4>3@5;5< (482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

4=>G0A=5 70AB>AC20==O V=H8E ?@5?0@0BV2.
A:V;L:8 ;:>?V4>3@5; ?5@5B2>@NTBLAO C A2V9 0:B82=89<5B01>;VB G0AB:>2> ?V4 4VTN CYP2C19,
B> 70AB>AC20==O ?@5?0@0BV2, O:V 7=86CNBL 0:B82=VABL FL>3> D5@<5=BC, =09V<>2V@=VH5,
?@872545 4> 7=865==O :>=F5=B@0FVW 0:B82=>3> <5B01>;VBC ;:>?V4>3@5;C 2 ?;071V6=89 70EV4
A;V4 C=8:0B8 >4=>G0A=>3> 70AB>AC20==O A8;L=8E B0 ?>@V2 CYP2C19 (482. @>74V;8
«A>1;82>ABV 70AB>AC20==O» B0 «\$0@<0:>:V=5B8:0»).

> ?@5?0@0BV2, I> ?@83=VGCNBL 0:B82=VABL CYP2C19, =0;560BL <5?@07>;, 57><5?@07>;,
D;C2>:A0:A5B8=, <:>:15@8:>=07>;, D;C:>=07>;, B8;:>?V48=, F8?@>D;>:A0F8=, F8<5B848=, .0@10
<075?V=, >:A:0@1075?V= B0 E;>@0;
=3V1VB>@8 ?@>B>==>W ?><5?@07>; C 4>7V 80 <3 1 @07 =0 4>1C, ?@8 AC?CB=L>AC20==V 7
;:>?V4>3@5;5< 01> 2 <560E 12 3>48= <0<8 F8E 42>E ?@5?0@0BV2, 7=86C202 :>=F5=B@0FVN
0:B82=>3> <5B01>;VBC C :@>2V =0 45 % (=020=B06C20;L=0 4>70) V 40 % (?V4B@870). &5 7=865==O
AC?@>2>46C20;>AO 7<5=H5==O< ?@83=VG5==O 03@530FVW B@<1>F8BV2 =0 39 %
(=020=B06C20;L=0 4>70) V 21 % (?V4B@870). GV:CTBLAO, I> 2 0=0;>3VG=C 270T<>4VN 7
;:>?V4>3@5;5< 2ABC?0B8<5 V 57><5?@07>;.

5=H 28@065=5 7=865==O :>=F5=B@0FV9 <5B01>;VBC C :@>2V A?>AB5@V30;>AO ?@8
70AB>AC20==V ?0=B>?@07>;C 01> ;0=A?@07>;C.
@8 >4=>G0A=>AC20==V ?0=B>?@07>;C C 4>7V 80 <3 1 @07 =0 4>1C ?;07<0B8G=V :>=F5=B@0FVW
0:B82=>3> <5B01>;VBC 7<5=H8;8AO =0 20 % (=020=B06C20;L=0 4>70) B0 =0 14 % (?V4B@870). &5
7=865==O AC?@>2>46C20;>AO 7<5=H5==O< A5@54=L>3> ?>:07=8:0 ?@83=VG5==O 03@530FVW B@>
<1>F8BV2 =0 15 % B0 11 %, 2V4?>2V4=>. B@8<0=V @57C;LB0B8 2:07CNBL =0 <>6;82VABL
>4=>G0A=>3> 70AB>AC20==O ;:>?V4>3@5;C B0 ?0=B>?@07>;C.
><1V=0FVO 7 V=H8<8 ;V:0@AL:8<8 70A>10<8. C;> ?@>2545=> @04 ;:V=VG=8E 4>A;V465=L 7
;:>?V4>3@5;5< B0 V=H8<8 ?@5?0@0B0<8 4;O 282G5==O ?>B5=V9=8E D0@<0:>48=0W 270T<>4VW
?@8 70AB>AC20==V ;:>?V4>3@5;C >4=>G0A=> 7 0B5=>;>;<, =VD548?V=>< 01> 7 >1><0
?@5?0@0B0<8 28O2;5=> =5 1C;>. @V< B>3>, D0@<0:>48=0?V4>3@5;C 70;8H8;0AO ?@0:B8G=> =57N
?@8 >4=>G0A=>AC20==V 7 D5=>10@1VB0;><, F8<5B848=>< B0 5AB@>35=><.
\$0@<0:>:V=5B8G=V 2;0AB82>ABV 483>:A8=C 01> B5>DV;V=C=5 74=>G0A=>AC20==V 7
;:>?V4>3@5;5=B0F84=V 70A>18 =5 2?;820;8 =0 @V25=L 01A>@1FVW ;:>?V4>3@5;C.
0=V, >B@8<0=V 2 E>4V 4>A;V465=L A>< ?5GV=:8 ;N48=8, A2V4G0BL ?@> B5, I> :0@1>:A8;L=V
<5B01>;VB8 ;:>?V4>3@5;C <>6CBL ?@83=VGC20B8 0:B82=VABL F8B>E@>450 2!9. &5 <>65
?>B5=V9=> ?V428IC20B8 @V2=V 2 ?;071V2, O: D5=VB>W= V B>;1CB0 B0 , O:V
<5B01>;V7CNBLAO 70 4>?><3>N F8B>E@>450 2!9. 572060NG8 =0 F5, @57C;LB0B8 4>A;V465==O
CAPRIE A2V4G0BL, I> D5=VB>W= V B>;1CB0
0 28=OB:>< V=D>@<0FVW I>4> 270T<>4VW 7V A?5F8DVG=8<8 ;V:0@AL:8<8 70A>10<8, =02545=>W
28I5, 4>A;V465==O I>4> 270T<>4VW ;:>?V4>3@5;C 7 ;V:0@AL:8<8 70A>10<8, O:V 70728G09
?@87=0G0NBL E2>@8< =0 0B5@>B@<1>7, =5 ?@>2>48;8AO. 4=0: ?0FVT=B8, O:V 1@0;8 CG0ABL C
;:V=VG=8E 4>A;V465==OE ;:>?V4>3@5;C, 70AB>A>2C20;8 >4=>G0A=> V=HV ?@5?0@0B8, 2;;NG0NG8
4VC@5B8:8, 15B0-1;>:0B>@8, V=3V1VB>@8 0=3V>B5=78=:>=25@BCNG>3> D5@<5=BC,
0=B03>=VAB8 :0;LFFVN, 70A>18, I> 7=86CNBL @V25=L E>;5AB5@8=C, :>@>=0@=V
207>48;0B0B>@8, 0=B84V015B8G=V 70A>18 (2;;NG0NG8 V=AC;V=), ?@>B85?V;5?B8G=V 70A>18,
3>@<>=>70=VAB8 GPIIb/IIIa, 157 >7=0: ;:V=VG=> 7=0GCI>W ?>1VG=>W 4VW.

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

\$0@<0:>48=0

5E0=V7< 4VW. ;:>?V4>3@5; A5;5:B82=> ?@83=VGCT 72O7C20==O 045=>78=48D>AD0BC (\$) 7
@5F5?B>@<< =0 ?>25@E=V B@<1>F8B0 B0 ?>40;LHC 0:B820FVN :> GPIIb/IIIa ?V4 4VTN \$ V B0:8<
G8=>< ?@83=VGCT 03@530FVN B@<1>F8BV2. ;O CB2>@5==O 0:B82=>W V=3V1VFW 03@530FVW
B@<1>F8BV2 =5>1EV4=0 1V>B@0=AD>@<0FVO ;:>?V4>3@5;C. ;:>?V4>3@5; B0:>6 ?@83=VGCT
03@530FVN B@<1>F8BV2, V=4C:>20=C V=H8<8 03>=VAB0<8, H;OE< 1;>:C20==O ?V428I5==O
0:B82=>ABV B@<1>F8BV2 282V;L=5=8< \$. ;:>?V4>3@5; =5>1>@>B=> <>48DV:CT \$-@5F5?B>@8 B@>

<1>F8BV2. B65, B@<1>F8B8, I> C2V9H;8 C 270T<>4VN 7 ;:>?V4>3@5;5<, 7 :V=FO WE 68BBT2>3> F8::;C. >@<0;L=0 DC=:FVO B@<1>F8BV2 2V4=>2;NTBLAO 7V H284:VABN, I> 2V4?>2V40T H284:>ABV >=>2;5==O B@<1>F8BV2.

\$0@<0:>48=0 ?5@H>3> 4=O 70AB>AC20==O C ?>2B>@=8E 4>1>28E 4>70E 75 <3 ?@5?0@0BC 28O2;OTBLAO ACBBT25 C?>2V;L=5==O \$-V=4C:>20=>W 03@530FVW B@<1>F8BV2. &O 4VO ?@>3@5A82=> ?>A8;NTBLAO V AB01V;V7CTBLAO 1>2>W 4>78 75 <3 AB0=>28BL 2V4 40 % 4> 60 %. 3@530FVO B@<1>F8BV2 V B@820;VABL :@>2>B5GV ?>25@B0NBLAO 4> ?>G0B:>2>3> @V2=O C A5@54=L>

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

A<:>:BC20==O

VA;O ?@89<0==O 2=CB@8H=L> >4=>@07>2>W B0 1030B>@07>28E 4>7 75 <3 =0 4>1C ;:>?V4>3@5; H284:> 2A<:>:BCTBLAO. !5@54=V <0:A8<0;L=V :=F5=B@0FVW 2 ?;07 =573> ;:>?V4>3@5;C (1;87L:>

2,2-2,5 =3/<; ?VA;O >4=>@07>2>W 4>78 75 <3) 4>AO30;8AO ?@81;87=> G5@57 45 E2 ?VA;O ?@89 <0==O 4>78. 1A>@1FVO AB0=>28BL =5 <5=H5 50 %, O: ?>:07CT 5:A:@5FVO <5B01>;V BV2 ;:>?V4>3@5;C V7 A5G5N.

>7?>4V;

;:>?V4>3@5; V >A=>2=89 (=50:B82=89) <5B01>;VB, I> F8@:C;NT 2 :@>2V, *in vitro*>1>@>B=> 72O7CNBLAO 7 1V;;0<8 ?;07<8 ;N48=8 (98 % V 94 %, 2V4?>2V4=>). &59 72O7>: 70;8H0TBLAO =5=0A8GC20=8< *in vitro*2 <560E H8@>:>3> 4V0?07>=C :=F5=B@0FV9.

5B01>;V7<

;:>?V4>3@5; 5:AB5=A82=> <5B01>;V7CTBLAO 2 ?5GV=FV. *In vitro* B0 *in vivo* VA=CT 420 >A=>2=8E H;OE8 9>3> <5B01>;V748= 2V41C20TBLAO 70 CG0ABN 5AB5@07 B0 ?@82>48BL 4> 3V4@>;V7C 7 CB2>@5==O <=50:B82=>3> ?>EV4=>3> :0@1=>=>2>W :8A;>B8 (O:5 AB0=>28BL 85 % 2V4 CAVE <5B01>;V BV2, I> F8@:C;NNBL C ?;07 V=H>3> 70;CG5=V D5@<5=B8 A8AB5<8 F8B>E@>G0B:C ;:>?V4>3@5; ?5@5B2>@NTBLAO =0 ?@>:A>:;>?V4>3@5;C CB2>@NTBLAO BV>;>25 ?>EV4=5 0:B82=89 <5B01>;VB. *In vitro* F59 <5B01>;VG=89 H;OE ?>A5@54:>20=89 D5@<5=B0<8 CYP3A4, CYP2C19, CYP1A2 B0 CYP2B6. :B82=89 <5B01>;VB ;:>?V4>3@5;C (BV>;>25 ?>EV4=5), O:89 1C2 284V;5=89 *in vitro*, H284:> B0 =572>@>B=> 72O7CTBLAO 7 @5F5?B>@0<8 =0 B@<1>F8B0E, B8< A0<8 < ?5@5H:>460NG8 03@530FVW B@<1>F8BV2.

82545==O

'5@57 120 3>48= ?VA;O ?@89> 3> 14C-;>?V4>3@5;C C ;N48=8 ?@81;87=> 50 % 48;>AO V7 A5G5N V 1;87L:> 46 % - 7 :0;>@0;L=>3> ?@89<0==O >4=>@07>2>W 4>78 75 <3 ?5@V>4 =0?V2282545==O ;:>?V4>3@5;C AB0=>28BL 1;87L:> 6 3>48=. 5@V>4 =0?V2282545==O >A=>2=>3> (=50:B82=>3>) <5B01>;VBC, I> F8@:C;NT 2 :@>2V, AB0=>28BL 8 3>48= ?VA;O >4=>@07>2>3> V 1030B>@07>2>3> ?@89>

\$0@<0:>35=5B8:0. CYP2C19 15@5 CG0ABL 2 CB2>@5==V O: 0:B82=>3> <5B01>;VBC, B0: V ?@>3> <5B01>;VBC 2->:A>:;>?V4>3@5;C. \$0@<0:>:V=5B8:0 0:B82=>3> <5B01>;VBC ;:>?V4>3@5;C B0 0=B8B@<1>F8B0@=V 5D5:B8, 70 40=8<8 28<1>F8BV2 *ex vivo*, 2V4@V7=ONBLAO 70;56=> 2V4 35=>B8?C CYP2C19.

;5;L CYP2C19*1 2V4?>2V40T ?>2=VABN DC=:FV>=CNG>4V O: 0;5;V CYP2C19*2 B0 CYP2C19*3 2V4?>2V40NBL =5DC=:FV>=CNG>2V40;L=8<8 70 1V;LHVABL 0;5;59, I> >A;01;NNBL DC=:FVN, C ?0FVT=BV2 T2@>?5>W4=>W (85 %) B0 <=>3>;>W4=>W (99 %) @0A 7V 7=865=8< <5B01>;V7<> FV9>20=V 7 2V4ACB=V< 01> >A;01;5=8< <5B01>;V7<><, 7CAB@VG0NBLAO 7=0G=> @V4H5. > =8E =0;560BL CYP2C19*4, *5, *6, *7, B0 *8. 0FVT=B 7V 7=865=8< <5B01>;V7<>< <0T 420 =5DC=:FV>=0;L=8E 0;5;V, O: 707=0G5=> 28I5. 3V4=> V7 >?C1;V:>20=8<8 40=8<8 35=>B8?8 CYP2C19, O:V 2V4?>2V40NBL 7=865=>?5>W4=>W @0A8, 4 % ?0FVT=BV2 =53@>W4=>W @0A8 B0 14 % ?0FVT=BV2 :8B09AL:>W =0FV>=0;L=>ABV. 0@07 VA=CNBL B5AB8, O:V 4>72>;ONBL 287=0G8B8 35=>B8? CYP2C19.

A>1;82V :0B53>@VW ?0FVT=BV2. \$0@<0:>:V=5B8:0 0:B82=>3> <5B01>;VBC ;:>?V4>3@5;C =5 4>A;V46C20;0AO C =86G5707=0G5=8E >A>1;828E :0B53>@V9 ?0FVT=BV2.

8@:>20 =54>AB0B=VABL. VA;O @53C;O@=>3> 70AB>AC20==O 75<3 ;:>?V4>3@5;C =0 4>1C ?0FVT=B0<8 V7 BO6:>N =8@:>2>N =54>AB0B=VABN (;V@5=A :@50B8=V=C 5-15 <:/=0 E28;8=C) V=3V1C20==O

\$-V=4C:>20=>W 03@530FVW B@<1>F8BV2 1C;> <5=H 28@065=8< (25 %) ?>@V2=O=> V7 B0:8< 65
5D5:B>< C 74>@>28E 4>1@>2>;LFV2, 0 G0A :@>2>B5GV 1C2 ?>4>265=89 <0965 B0: A0<>, O: V C
74>@>28E 4>1@>2>;LFV2, O:V >B@8@>H>N 2 CAVE ?0FVT=BV2.

5GV=:>20 =54>AB0B=VABL. VA;O @53C;O@=>3> ?@89>

0A>20 ?@8=0;56=VABL.>H8@5=VABL 0;5;59 CYP2C19, O:V A?@8G8=ONBL ?@>

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

A=>2=V DV78:>-EVABV: B01;5B:8, 2:@8BV ?;V2:>2>N >1>;>=:>N, >@0=652V, :@C3;V, 42>>?C;;V.

"5@ABV.2 @>:8.

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

#?0:>2:0. > 10 B01;5B>: C 1;VAB5@V, ?> 1 3 B0 10 1;VAB5@V2 C ?0GFV.

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

8@>1=8:. \$;0 \$0@<0ALNB8:0;A B4. / Flamingo Pharmaceuticals Ltd.

VAF57=0E>465==O.

.@848G=0 04@5A0:

7/1, >@?>@59B 0@:, !V>=-"@><109 >04, '5<1C@, C<10W 400071, =4VO/

7/1, Corporate Park, Sion-Trombay Road, Chembur, Mumbai - 400071, India.

4@5A0 1=8FB20:

-28, ??, \$0T@ @V3594, ...!., "0;>460, 09>= 09304, 0E0@0HB@0, 410208, =4VO/

E-28, Opp. Fire Brigade, M.I.D.C., Talaja, Dist. Raigad, Maharashtra, IN-410208, India.

002=8:. =0=B0 54V:50@ B4./Ananta Medicare Ltd.

VAF57=0E>465==O.

!LNB 1, 2 !B59H= >@B,04, \$C;E0<, >=4>=, 5;8:0 @8B0=VO/

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