

!" #&/

4;O <548G=>3> 70AB>AC20==O ?@5?0@0BC

\$!®

(VARFAREX)

4:

7G0 @5G>28=0: 20@D0@8= (warfarin);

01;5B:0

>28=8: ;0:B>70, <=>3V4@0B; F5;N;>70 :@8AB0;VG=0; :@>A?>2V4>=; <03=VN AB50@0B; V=483>:0@: 3 <3)

PC=F>289 4R (124) (4;O B01;5B>: 5 <3).

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

><0:>B5@0?52B8G=0 3@C?0. =B8B@><1>B8G=V 70A>18. =B03>=VAB8 2VB0

! 0103.

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

70==O.

>DV;0:B8:0 B0 ;V:C20==O B@<1>7C 3;81>:8E 25= V 5<1>;VW ;535=52>W 0@B5@VW;

>@8==0 ?@>DV;0:B8:0 V=D0@:BC :0@40 V ?@>DV;0:B8:0 B@<1>5<1>;VG=8E CA::04=5=L (V=AC;LB 01>

8AB5<=0 5<1>;VO) ?VA;O V=D0@:BC:0@40;

>DV;0:B8:0 B@<1>5<1>;VG=8E CA::04=5=L C ?0FVT=BV2 V7 DV1@8;OFVTN ?5@54A5@4O, C@065==O<

5@F528E ;:0?0=V2 01> 7 ?@>B57>20=8<8 ;;0?0=0<8 A5@FO;

>DV;0:B8:0 H284:<8=CG8E VH5

>B8?>:070==O.

28I5=0 GCB;82VABL 4> 20@D0@8=C B0/01> 4> 1C4L-O:>W 4>?>W @5G>28=8 ?@5?0@0BC;

=VG=> 2AB0=>2;5=0 :@>2>B5G0;

E8;L=VABL 4> :@>2>B5G (E2>@>10 V;;51@0=40, 35<>DV;VO, B@<1>F8B>?5=VO B0 ?>@CH5==O DC=:FV9

@<1>F8BV2);

D C=8:=5==O @878:C @>728B:C B06:8E :@>2>B5G ?@>BO3<< 72 3>48= ?VA;O >1H8@=8E >?5@0B82=8E

@CG0=L, ?@>BO3<< 48 3>48= C ?VA;O?>;>3>2>4V;

06:0 =8@:>20 V ?5GV=:>20 =54>AB0B=VABL 01> F8@>7 ?5GV=:8;

;V:>20=0 01> =5:>=B@>;L>20=0 0@B5@V0;L=0 3V?5@B5=7VO;

I>402=O V=B@0:@0=V0;L=0 :@>2>B5G0; AB0=8, I> 28;;8:0NBL V=B@0:@0=V0;L=C :@>2>B5GC, =0?@8;;04

52@87<0 <>7:>28E 0@B5@V9, 0=52@87<0 0>@B8;

E8;L=VABL 4> =5?@8B<=>ABV (?04V==O);

5@0FVW =0 F5=B@0;L=V9 =5@2>2V9 A8AB5=0 >G0E;

C=:>2>:-8H:>2V 01> =8@:>2V :@>2>B5GV B0 WE CA::04=5==O;

25@B8:C;L>7;

>O:VA=V ?CE;8=8;

@8:>7=5 @>7H8@5==O 25= AB@02>E>4C;

=D5:FV9=89 5=4>:0@48B, ?5@8:0@48B 01> 5:AC40B82=89 ?5@8:0@48B;

80=, ?@8 O:>

<10;L=0 ?C=:FVO.

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

@D0@5:A® =5>1EV4=> 70AB>A>2C20B8 2 >48= V B>9 A0<89 G0A.

C 0@D0@5:AC® 287=0G0NBL 4;O :>6=>3> ?0FVT=B0 V=482V4C0;L=>, :5@CNG8AL ?>:07=8:0<8

5=0@>4=>3> =>@<0;V7>20=>3> 2V4=>H5==O () ?@>B@><1V=C.

?07>= FV;L>2>3> ?@8 B5@0?VW ?5@>@0;L=8<8 0=B8:>03C;O=B0<8.

>DV;0:B8:0 B@<1>5<1>;VG=8E CA::04=5=L C ?0FVT=BV2 7 ?@>B57>20=8<8 ;;0?0=0<8 A5@FO:

-3,5. =HV ?>:070==O: 2,0-3,0.

@>A;V. 0FVT=B0< 7 =>@<0;L=>N <0A>N BV;0 B0 28EV4=8< =86G5 1,2 A;V4 70AB>A>2C20B8

<3/45=L 20@D0@8=C (2 B01;5B:8 ?> 5 <3) ?@>BO3×< 3-E 4=V2. >40;LHV 4>78, 15@CG8 4> C2038 @V25=L =0
9 45=L, ?@54AB02;5=V 2 B01;8FV 1.
<5=4>20=0 ?>G0B:>20 4>70 4;O 0<1C;0B>@=8E ?0FVT=BV2 B0 ?0FVT=BV2 V7 2@>465=8< 45DVF8B>< ! 01>
V;;0 AB0=>28BL 5<3/45=L 20@D0@8=C (*)?@>BO3×< 3-E 4=V2. >40;LHV 4>78, 15@CG8 4> C2038 @V25=L
4-9 45=L, ?@54AB02;5=V 2 B01;8FV 1.
VT=B8 ;VB=L>3> 2V:C, ?0FVT=B8 7V 7=865=>N<0A>N BV;0.
<5=4>20=0 ?>G0B:>20 4>70 AB0=>28BL 5<3/45=L 20@D0@8=C (*) ?@>BO3×< 2-E 4=V2. >40;LHV 4>78,
00E>2CNG8 @V25=L =0 3-9 45=L, ?@54AB02;5=V 2 B01;8FV 1.
VT=B8 7 ?>G0B:>28< 28I5 1,2, ?0FVT=B8 7 70E2>@N20==O<8 0I> O:V 70AB>A>2CNBL ?@5?0@0B8, I>
:820NBL =0 5D5:B82=VABL B5@0?VW 0=B8:>03C;O=B0<8.
<5=4>20=0 ?>G0B:>20 4>70 AB0=>28BL 5<3/45=L 20@D0@8=C (*) ?@>BO3×< 2-E 4=V2. >40;LHV 4>78,
@CG8 4> C2038 @V25=L =0 3-9 45=L, ?@54AB02;5=V 2 B01;8FV 1.

"01;8FO 1

5=L	
>70 20@D0@8=C, <3/45=L	
1	
-	
10 (5,0*)	

2
-
10 (5,0*)

2,5-4,0	
> 4,0	
10 (5,0*)	
5	
3	
2,5	
1,5	
?@>?CAB8B8 >48= 45=L	

4 -6
< 1,4
1,4-1,9
2,0-2,4
2,5-2,9
3,0-3,9
4,0-4,5

10
7,5
5
4,5
3
?@>?CAB8B8 >48= 45=L, ?>BV< 1,5
?@>?CAB8B8 2 4=V, ?>BV< 1,5

0820;VABL;C@AC;V:C20==O 287=0G0TBLAO V=482V4C0;L=> (2V4 6-B8 B86=V2 4> 70AB>AC20==O
>BO3>:CAL>3>68BBO). # 28?04:C 28=8:=5==O B>;5@0=B=>ABV 4> 4VW 0@D0@5:AC® 4>78 >AB0==L>3>
1V;LH8B8=0 20 %
?CA:0BBLAO ?V4281C20B8 C 2-10 @07V2. 1A>;NB=> =5>1EV4=8< T AC2>@5 4>B@8<0==O @5:><5=40FV9
1V;LH8B8=0 10 %
:0@O2V4 0 A=> 70AB>AC20==O ?@5?0@0BC B0 @5B5;L=89 ;01>@0B>@=89 :>=B@>;L 70 ?>:07=8:0<8
>@B0=1Q5@>2V
5=H8B8=0 10 %
V4 2863;545=L 4>4>AQ3=5==Q AB01V;L=>3>FV;L>2>3>@V2=Q 70728G09 F5 2V41C20TBLAO ?@>BO3×
(@>?CAB8B8 4><4,5; ?>BV< ?@>4>268B8 7 4>7>N,1><5=H5 =0 20 %
5 4=V2 7 ?>G0B:C ;V:C20==O. 0;V V=B5@20; G0B>: 70AB>AC20==O =>28E ?@5?0@0BV2 01> ?@8?8=5==O

AB>AC20==O :>;8H=VE ?>B@51CT 1V;LH G0AB>3> 287=0G5==O . @8 B@820;>7C 20@D0@8=C (7030;L=0
70 20@D0@8=C, O:C ?0FVT=B >B@8BO3>< B86=O) 2V4?>2V4=> 7 B01;8F5N 1. @8 =5>1EV4=>ABV 778
ABC?=5 282>4OBL G5@57 1 01> 2 B86=V. >BV< V=B5@20; 7=>2C <>6=0 ?>ABC?>2> 71V;LHC20B8 4> 4
6=V2.
8?04:C =5>1EV4=>ABV H284:>3> 0=B8B@><1VG=>3> 5D5:BC @5:><5=4CTBLAO ?>G8=0B8 ;V:C20==O V7
545==O 35?0@8=C. >BV< 22545==O 35?0@8=C ?@>4>26CNBL 7 >4=>G0A=8< ?@89><>< 20@D0@8=C
>>BO3>< 5-7 4=V2, 4>:8 =5 1C45 715@V30B8AO =0 FV;L>2>BO3>< O:
8. >G0B>: B0 ?@>4>265==O B5@0?VW 0=B8:>03C;O=B0<8 C 4VB59 ?@>2>48BLAO ?V4 A?>AB5@565==O<
4V0B@V2. >7C <>6=0 ?V4V1@0B8 2V4?>2V4=> 4> B01;8FV 2.

"01;8FO 2

1-9 45=L

/:I> 107>25 7=0G5==O 2V4 1,0 4> 1,3, B> ?>G0B:>20 4>70
AB0=>28BL 0,2 <3/:3 <0A8 BV;0, ?@8 ?>@CH5==V DC=:FVW
?5GV=:8 0,1 <3/:3 <0A8 BV;0

=V 7 2-3> ?> 4-9, O:I> 7=0G5==O

:

2V4 1,1 4> 1,3

2V4 1,4 4> 1,9

2V4 2,0 4> 3,0

2V4 3,1 4> 3,5

>3,5

V4B@870:

?>2B>@8B8 4>7C =0A8G5==O

50 % 2V4 ?>G0B:>2>W 4>78

50 % 2V4 ?>G0B:>2>W 4>78

25 % 2V4 ?>G0B:>2>W 4>78

4>G5:0B8AO 4>AO3=5==O <3,5, ?>BV< 2V4=>28B8

;V:C20==O 4>7>N, I> AB0=>28BL 50 % 2V4 ?>?5@54=L>W

4>78

V4B@8 7=0G5==O :

2V4 1,1 4> 1,4

2V4 1,5 4> 1,9

2V4 2,0 4> 3,0

2V4 3,1 4> 3,5

>3,5

VW (B86=520 4>70):

71V;LH8B8 =0 20 %

71V;LH8B8 =0 10 %

4>7C =5 7

7<5=H8B8 =0 10 %

4>G5:0B8AO 4>AO3=5==O <3,5, ?>BV< 2V4=>28B8

;V:C20==O 4>7>N, <5=H>N =0 20 % 2V4 ?>?5@54=L>W 4>78

=>2V>?5@0FVW.5@54-,?@8-B0?VA;O>?5@0FV9=00=B8:>03C;O=B=0B5@0?VO74V9A=NTBLAO
ABC?=8<G8=>
=0G8B870B8645=L4>?;0=>2>W>?5@0FVW.
-54=V24>>?5@0FVW?@8?8=8B8?@89><20@D0@8=C.:/I>C?0FVT=B028A>:89@878:28=8:=5==OB@>
>7C,?@>DV;0:B8G=>225AB8?V4H:V@=>=87L:><;5:C;O@=>8935?0@8=. @8?8=5==O70AB>AC20==O
@D0@8=C70;568BL2V4. @89><20@D0@8=C?@8?8=ONBL:
7054=V24>>?5@0FVW,O:I>>4,0;
7034=V4>>?5@0FVW,O:I>3,0-4,0;
7024=V4>>?5@0FVW,O:I>2,0-3,0.
5G5@V?5@54>?5@0FVTN287=0G8B8.:/I>>1,8,?5@>@0;L=>01>2=CB@VH=L>25==>225AB80,5-1,0<3
B01.>?5@0FV9=8945=L>FV=8B8V=DC7VN=5D@0:FV>=>20=>3>35?0@8=C01>?@>DV;0:B8G=5
545==O=87L:><;5:C;O@=>3>35?0@8=C.
>B03><5-74=V2?VA;O>?5@0FVW>4=>G0A=>72V4=>2;5==O<B5@0?VW20@D0@8=><?@>4>268B8
4H:V@=522545==O=87L:><;5:C;O@=>3>35?0@8=C.
8<0;8E>?5@0FVOE2V4=>28B870AB>AC20==O20@D0@8=C C728G09=V9?V4B@87V225G5@V
5@0FV9=>3>4=O,?@825;8:8E>?5@0FVOEC45=L, :>;82V4=>2;NNBL5=B5@0;L=5E0@GC20==O.

VG=V@50:FVW.
G5=02545=V=51060=V?>1VG=V@50:FVW,?@>O:V?>2V4><;O;>AO.
>2>20A8AB5<0:AC14C@0;L=035<0B><0,30@OG:0.
>2>=>A=0B0:@>2>B2>@=0A8AB5<0:35<>@03VO,:C<0@8=>289=5:@>7,7010@2;5==O?0;LFV2=V3C
@?C@>289>;V@,?C@?C@0,5>78=>DV;VO,20A:C;VB,0=5
0;L=0A8AB5<0,3@C4=0.;VB8=0B0A@54>AB5=VO:0;LF8DV:0FVOB@0E5W,35<>B>@0:A.
C=:>2>-.8H:>289B@0:B:=C4>B0,1;N20==O,1;N20==O:@>2N,4V0@5O,1V;LC4V;O=FV682>B0,H;C=:>2>-
H:>20:@>2>B5G0,:@>2>B5G07?@O<>W:8H:8,<5;5=0.
V=:0,6>2G>282V4=V?@>B>:8:>1>@>B=5?V428I5==O0:B82=>ABVD5@<5=BV2?5GV=:8,E>;5AB0B8G=89
?0B8B,6>2BO=8FO.
V@0B0?V4H:V@=VB:0=8=8:>1>@>B=00;>?5FVO,28A8?0==O,:@>?82O=:0,A25@1V6,5:75<0,5@8B5
B>7=89=01@O:H:V@8,I>?@872>48BL4>5:EV<>7C,V=D0@:BCB0=5:@>7CH:V@8.
G>AB0B520A8AB5<0:35<0BC@VO,?@V0?V7
30;L=V:0;5@3VG=V@50:FVW(70728G09C283;04V28A8?0=L=0H:V@V),=5D@8B,C@>;V BV07,
C1C;O@=>89=5:@>7.
G0ABVH8<8?>1VG=8<8O28I0<820@D0@8=C T:@>2>B5G0B0:@>2>28;828,7>:@5<0:=57=0G=V=>A>2V
>2>B5GV B0:@>2>B5GV7OA5=,?V4H:V@=V:@>2>28;828;@V4:>2=CB@VH=L>G5@5?=V,H;C=:>2>-
H:>2V:@>2>B5GV.09G0ABVH89D0:B>@ @878:C V=B@0:@0=V0;L=>W:@>2>B5GV=5;V:>20=001>
:=B@>;L>20=03V?5@B5=7VO.>6;82VABL:@>2>B5GV71V;LHCTBLAO,O:I>7=0G=>28I8970FV;L>289
V25=L.:/I>:@>2>B5G0?>G0;0AO?@8=01060=>2>70728G09T?>1VG=570E2>@N20==O01>AB0=,I>
B@51CT4>A;V465==O.02VBL C28?04:C=57=0G=>W:@>2>B5GV=5>1EV4=>?@>V=D>@F5;V:0@O.
0@8=>289=5:@>7@V4:VA=5CA;;04=5==O?@8;V:C20==V20@D0@8=>770728G09?>G8=0TBLAO7
?8?CE;>ABVH:V@8=86=VE:V=FV2>;01>AV4=8FL,I>?>B5<=V;8,0B0:>6CV=H8EBV<C@065==O
30NBL=5:@>B8G=8<8.#90%28?04:V2=5:@>7@>72820TBLAO C6V=>;C@065==OA?>AB5@V30NBLAO7
>3>?>10-945=L?@89>;>3VO?5@5410G0T45DVF8B1V;;0!01>S.@>465=0=54>AB0B=VABL F8E1V;;V2<>65
B8?@8G8=>NCA;;04=5=L,B><20@D0@8=C?>28=5=1CB8@>7?>G0B89>4=>G0A=>V722545==O<
?0@8=C B0<0;8<8?>G0B:>28<84>70<8?@5?0@0BC.:/I>28=8:0TCA;;04=5==O,B>?@89><20@D0@8=C
?8?8=ONBLB0?@>4>26CNBL22545==O35?0@8=C4>703>T==OB0@C1FN20==OC@065=L.
0@2;5==O?0;LFV2=V3C?C@?C@>289>;V@I51V;LH@V4:VA=5CA;;04=5==O?@8B5@0?VW20@D0@8=>
2V:870B5@>A;;5@>7>5<1>;V9.8=8:0NBLA8<5B@8G=V?C@?C@>2VC@065==OH:V@8?0;LFV2B0
4>H>2AB>?,I>AC?@>2>46CNBLAO?5:CG8<1>;55<1>;V70FVOE>;5AB5@>;C,1V;LC682>BV,?0=:@50B8B,

VG=V4VW C4VB590=0;>3VG=VB0:8<C4>@>A;8E.>2>B5G0203><0?>1VG=04VO.V4:>28=8:0NBL
A8?0==O,0;>?5FVOB0=5:@>7H:V@8. @8B@820;>AC20==V@>72820TBLAO>AB5>?5=VO.

>54>7C20==O.
<8::@>2>B5GV,:@>2>B>G82VABL.
C20==O:C;53:8E28?04:0E?@8?>ABC?>2>7C20==V70728G094>AB0B=L>7=878B84>7C01>?@8?8=8B8

:C20==O 20@D0@8=< 4> ?>25@=5==O 4> FV;L>2>3> @V2=O. @8 3>AB@>7C20==V ?@5?0@0BC
>@>6=5==O H;C=:0 =5 @5:><5=4CTBLAO G5@57 @878: 28=8:=5==O :@>2>B5GV. !;V4 ?>2B>@=>
AB>A>2C20B8 0:B82>20=5 2C3V;;O 4;O 70?>1V30==O 01A>@1FVW B0 5=B5@>35?0B8G=>W
5F8@:C;OFVW 20@D0@8=C. @8 70AB>AC20==V 0:B82>20=>3> 2C3V;;O ?0@5=B5@0;L=> (2/2) A;V4 225AB8
B0728B:C :@>2>B5GV 4VN 20@D0@8=C A;V4 ?@8?8=8B8, 70AB>A>2CNG8 2VB025==> 2 4>7V 5-10 <3),
=F5=B@0B D0:B>@0 73>@B0==O 01> A2V6C 70<>@>65=C ?;071EV4=>ABV ?>40;LH>W 0=B8:>03C;OFVW
>1EV4=> C=8:0B8 70AB>AC20==O 2VB07V 1V;LH5 10<3. V=H>
<<5=40FVW I>4> ;V:C20==O ?5@54>7C20==O ?@54AB02;5=V C B01;8FV 3.

"01;8FO 3

V25=L

5:><5=40FVW

@8 2V4ACB=>ABV ;;V=VG=> 7=0GCI>W :@>2>B5GV

< 5,0

@>?CAB8B8 =0ABC?=C 4>7C 20@D0@8=C B0 2V4=>28B8 B5@0?VN
=86G>N 4>7>N ?VA;O =>@<0;V70FVW

@>?CAB8B8 =0ABC?=V 1-2 4>78 20@D0@8=C B0 2V4=>28B8 B5@0?VN
=86G>N 4>7>N ?VA;O =>@<0;V70FVW 01> ?@>?CAB8B8 =0ABC?=C 4>7C
B0 ?5@>@0;L=> 70AB>AC20B8 2,5 <3 2VB0

@8?8=8B8 70AB>AC20==O 20@D0@8=C B0 ?5@>@0;L=> 70AB>AC20B8
3,0-5,0 <3 2VB0

@8 =5>1EV4=>ABV H284:>3> ?@8?8=5==O 4VW 20@D0@8=C (=0?@8;:04, ?5@54
>?5@0FVTN)

@8?8=8B8 70AB>AC20==O 20@D0@8=C B0 70AB>AC20B8 ?5@>@0;L=>
2,0-4,0 <3 2VB0 70 24 3>48=8 4> ?@>F54C@8, 4>40B:>2> ?V7=VH5 <>6=0
70AB>AC20B8 ?5@>@0;L=> I5 1,0-2,0 <3 2VB0

@8 =5>1EV4=>ABV 4C65 H284:>3> ?@8?8=5==O 4VW 20@D0@8=C

