

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

"
(DROTAVERIN□)

!;:04:

1 B01;5B:0

4VNG0 @5G>28=0: 4@>B025@8=C 3V4@>E;>@84 - 0,04 3;

4>?>28=8: F5;N;>70 :@8AB0;VG=0, :@>E<0;L :0@B>?;O=89, ;0:B>78 <=>3V4@0B, :@5<=VN 4V>:A84
:>;>W4=89 1572>4=89, :0;LFVN AB50@0B.

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

A=>2=V DV78:>-EVABV: B01;5B:8 :@C3;>W D>@<8 2V4 A2VB;>-6>2B>3> 4> B5<=>-6>2B>3>
:>;L>@C, V7 42>>?C;:>N ?>25@E=5N, 4>?CA:0TBLAO <0@2VABL.

\$0@<0:>B5@0?52B8G=0 3@C?0.

0A>18, O:V 70AB>A>2CNBLAO ?@8 DC=:FV>=0;L=8E H;C=:>2>-.8H:>28E @>7;040E.
>4 "% 03D02.

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

\$0@<0:>48=0 @>B025@8= ?>EV4=5 V7>EV=>;V=C, O:89 28O2;OT A?07<>;VB8G=C 4VN
157?>A5@54=L> =0 3;04:C < ?@83=VG5==O 4VW D5@<5=BC D>AD>4V5AB5@070 V (\$V), I>
A?@8G8=OT 71V;LH5==O :>=F5=B@0FVW F\$ V 7024O:8 V=0:B820FVW ;53:>3> ;0=FN6:0 :V=07878=C
(MLCK) 4> @>7A;01;5==O 3;04:>3> <'O70.

In vitro 4@>B025@8= ?@83=VGCT 4VN D5@<5=BC \$V V =5 2?;820T =0 4VN V7>D5@<5=BV2
D>AD>4V5AB5@078 (\$) V D>AD>4V5AB5@078 V (\$V). \$V <0T 25;8:5 DC=:FV>=0;L=5 7=0G5==O 4;O
7=865==O A:>@>GC20;L=>W 0:B82=>ABV 3;04:8E <O7V2, B>2V V=3V1VB>@8 FL>3> D5@<5=BC
<>6CBL 1CB8 :>@8A=8<8 4;O ;V:C20==O E2>@>1, O:V AC?@>2>46CNBLAO 3V?5@@CE;82VABN, 0
B0:>6 @V7=8E 70E2>@N20=L, ?V4 G0A O:8E 28=8:0NBL A?07<8 H;C=:>2>-.8H:>2>3> B@0:BC.
:;VB8=0E 3;04:8E <O7V2 :0@40 B0 AC48= F\$ 3V4@>;V7CTBLAO 7451V;LH>3> V7>D5@<5=B<< \$, B>
B025@8= T 5D5:B82=8< A?07<>;VB8G=8< 70A>1><, O:89 =5 <0T 7=0G=8E ?>1VG=8E 5D5:BV2 7 1>:C
A5@F52>-AC48==>W A8AB5<8 B0 A8;L=>W B5@0?52B8G=>W 4VW =0 FN A8AB5
@>B025@8= 5D5:B82=89 ?@8 A?07<0E 3;04:>W 2>3>, B0: V <O7>2>3> ?>E>465==O. @>B025@8= 4VT
=0 3;04:C 2>-.8H:>2>W, 1V;V0@=>W, A5G>AB0B52>W B0 AC48==>W A8AB5< =570;56=> 2V4 B8?C
WE=L>W 02B>=><=>W V==5@20FVW.

V= ?>A8;NT :@>2>>1V3 C B:0=8=0E 7024O:8 A2>W9 740B=>ABV @>7H8@N20B8 AC48=8.
VO 4@>B025@8=C T A8;L=VH>N 70 4VN ?0?025@8=C, 01A>@1FVO H284H0 B0 ?>2=VH0, 2V=<5=H5
72'O7CTBLAO 7 1V;;<8 A8@>20B:8 :@>2V. 5@5203>N 4@>B025@8=C T B0:>6 B5, I> =0 2V4VA;O
9>3> ?0@5=B5@0;L=>3> 22545==O =5 A?>AB5@V30TBLAO B0:>3> ?>1VG=>3> 5D5:BC O: AB8
\$0@<>:V=5B8:0. @>B025@8= H284:> B0 ?>2=VABN 01A>@1CTBLAO ?VA;O ?5@>@0;L=>3>
70AB>AC20==O. V= 28A>:>N N (95-98 %) 72O7CTBLAO 7 0;L1C A8@>20BFV :@>2V 4>AO30TBLAO
?@>BO3>< 45-60 E28;8= ?VA;O ?5@>@0;L=>3> 70AB>AC20==O. VA;O ?5@28==>3><5B01>;V7W 4>78
=04E>48BL 4> :@>2>>1V3C C =57
5B01>;V7CTBLAO C ?5GV=FV. 0?V2?5@V>4 1V>;>3VG=>3> VA=C20==O AB0=>28BL 8-10 3>48=.
0 72 3>48=8 4@>B025@8= ?@0:B8G=> ?>2=VABN 282>48BLAO 7 >@30=V750 % 282>48BLAO V7
A5G5N B0 ?@81;87=> 30 % 7 :0;>A=>2=>B025@8= 282>48BLAO C D>@@

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

>:070==O.

;V:C20;L=>N <5B>N ?@8:

- A?07<0E 3;04:>W 2O70=8E V7 70E2>@N20==O<8 1V;V0@=>3> B@0:BC: E>;5F8AB>;VBV07V,
E>;0=3V>;VBV07V, E>;5F8AB8BV, ?5@8E>;5F8AB8BV, E>;0=3VBV, ?0?V;VBV;

- A?07<0E 3;04:>W @N20==OE A5G>2>3> B@0:BC: =5D@>;V BV07V, C@5B5@>;V BV07V, ?VT;V BV, F8AB8BV, B5=57<0E A5G>2>3> /: 4>?>
- A?07<0E 3;04:>W 2>-.8H:>2>3> B@0:BC: 28@07:>2V9 E2>@>1V H;C=:0 B0 420=04FOB8?0;>W :8H:8, 30AB@8BV, :0@4V>- B0/01> ?V;>@>A?07;V BV, A?0AB8G=>;V BV V7 70?>@< V A8=4@>4@07=5=>3> :8H5G=8:C, I> AC?@>2>46CTBLAO <5B5>@87<<<;
- 3>;>2=>;N =0?@C65==O;
- 3V=5:>;>3VG=8E 70E2>@N20==OE (48A<5=>@5O).

@>B8?>:070==O.

V428I5=0 GCB;82VABL 4> 4@>B025@8=C 01> 4> 1C4L-O:>3> :>5=B0 ?@5?0@0BC. "O6:0 ?5GV=>20, =8@:>20 01> A5@F520 =54>AB0B=VABL(A8=4@<< <0;>3> A5@F52>3> 28:84C).

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

=3V1VB>@8 D>AD>4V5AB5@078, B0:V O: ?0?025@8=, 7=86CNBL 0=B8?0@:V=A>=VG=89 5D5:B ;52>4>?8. !;V4 7 >15@56=VABN 70AB>A>2C20B8 ?@5?0@0B @>B025@8= >4=>G0A=> 7 ;52>4>?>N, >A:V;L:8 0=B8?0@:V=A>=VG=89 5D5:B >AB0==L>W 7<5=HCTBLAO, 0 @83V4=VABL B0 B@5<>@ ?>A8;NNBLAO.

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

0AB>A>2C20B8 7 >A>1;82>N >15@56=VABN ?@8 0@B5@V0;L=V9 3V?>B5=7VW.
@5?0@0B @>B025@8= 7C. 5 70AB>A>2C20B8 4;O ;V:C20==O E2>@8E, O:V AB@0640NBL =0 @V4:VA=V A?04:>2V 70E2>@N20==O, B0:V O: =5?5@5=>A878, 45DVF8B ;0:B078 0??0 01> A8=4@<< <0;L01A>@1FVW 3;N:>78-30;0:B>78.

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

03VB=VABL. /: ?>:070;8 @57C;LB0B8 4>A;V465=L =0 B20@8=0E, ?5@>@0;L=5 70AB>AC20==O 4@>B025@8=C =5 A?@8G8=O;> 6>4=8E >7=0: 1C4L-O:>3> ?@O<<3> 01> =5?@O<<3> 2?;82C =0 203VB=VABL, 5<1@V>=0;L=89 @>728B>;, ?>;>38 01> ?VA;O?>;>3>289 @>728B>:. 4=0: =5>1EV4=> 7 >15@56=VABN ?@87=0G0B8 ?@5?0@0B 203VB=8< 6V=:0 >4C20==O 3@C44N. '5@57 2V4ACB=VABL 40=8E C ?5@V>4 3>4C20==O 3@C44N 70AB>AC20==O ?@5?0@0BC =5 @5:><5=4CTBLAO.

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.

/:I> ?VA;O 70AB>AC20==O ?@5?0@0BC A?>AB5@V30TBLAO 70?0<>@>G5==O, A;V4 C=8:0B8 :5@C20==O 02B><>1V;5< V 28:>=0==O @>1VB, I> ?>B@51CNBL ?V428I5=>W C2038.

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

>@>A;V: 728G09=0 A5@54=O 4>70 AB0=>28BL 120-240<3 =0 4>1C 70 2-3 ?@89><8.
@07V 70AB>AC20==O 4@>B025@8=C 4VBO
4;O 4VB59 2V:<< 6-12 @>:V2 <0:A8<0;L=0 4>1>20 4>70 AB0=>28BL 80 <3 (@>74V;5=0 =0 2 ?@89><8);
4;O 4VB59 2V:<< 2V4 12 @>:V2 <0:A8<0;L=0 4>1>20 4>70 AB0=>28BL 160 <3 (@>74V;5=0 =0 2-4 ?@89><8).

VB8. VBO< 2V:<< 4> 6 @>:V2 70AB>AC20==O ?@5?0@0BC ?@>B8?>:070=>.

0AB>AC20==O 4@>B025@8=C 4VBO< =5 >FV=N20;>AO C ;;V=VG=8E 4>A;V465==OE.

5@54>7C20==O.

/8<8: ?@8 7=0G=>7C20==V 4@>B025@8=C A?>AB5@V30;8AO ?>@CH5==O A5@F52>3> @8B 2V4=>ABV, 2 B>2=0 1;>:040 ?CG:0 VA0 B0 7C?8=:0 A5@FO, O:V<>6CBL 1CB8 ;5B0;L=8<8. @8 ?5@54>7C20==V ?0FVT=B ?>28=5= 7=0E>48B8AO ?V4 @5B5;L=8< A?>AB5@565==O< ;V:0@O B0 >B@8

>1VG=V @50:FVW.

>1VG=0 4VO, I> A?>AB5@V30;0AO ?V4 G0A ;:V=VG=8E 4>A;V465=L V,<>6;82>, 1C;0 A?@8G8=5=0
4@>B025@8=><, @>7?>4V;5=0 70 A8AB5<>N >@30=V2 B0 G0AB>B>N 28=8:=5==O: 4C65 ?>H8@5=V (
□ 1/10), ?>H8@5=V (□ 1/100, □1/10), =5?>H8@5=V (□ 1/1000, □1/100), ?>>48=>:V (□ 1/10000, □1/1000),
2:@09 ?>>48=>:V (□1/10000).

>@CH5==O VW A8AB5<8. >>48=>:V: 0;5@3VG=V @50:FVW, 2::NG0NG8 0=3V>=52@>B8G=89 =01@O.,
:@>?82O=:C, 28A8?0==O, A25@1V6, 3V?5@5?0A=8FN, >7=>1, ?V428I5==O B5
!5@F52>-AC48==V ?>@CH5==O. >>48=>:V: ?@8A:>@5=5 A5@F518BBO, 0@B5@V0;L=0
3V?>B5=7VO.

>@CH5==O =5@2>2>W A8AB5<8. >>48=>:V: 3>;>2=89 1V;L, 70?0<>@>G5==O, 157A>==O.
(;C=:>2>-:8H:>2V ?>@CH5==O. >>48=>:V: =C4>B0, 70?>@, 1;N20==O.

"5@ABV.3 @>:8.

5 A;V4 70AB>A>2C20B8 ?VA;O 70:V=G5==O B5@ABV, 707=0G5=>3> =0 C?0:>2FV.

#<>28 715@V30==O.

15@V30B8 C =54>ABC?=>

15@V30B8 2 >@83V=0;L=V9 C?0:>2FV ?@8 B50!.

#?0:>2:0.

> 10 B01;5B>: C 1;VAB5@V, ?> 1 01> 2 1;VAB5@8 C ?0GFV 7 :0@B>=C.

0B53>@VO 2V4?CA:C. 57 @5F5?B0.

8@>1=8:.

" <<%V

VAF57=0E>465==O 28@>1=8:0 B0 9>3> 04@5A020465==O 4VO;L=>ABV.

#: @0W=0, 61010, <. %0@:V2, 2C;. >@4VT=:V2AL:0, 1.

0O2=8:.

" <<%V

VAF57=0E>465==O 70O2=8:0 B0/01> ?@54AB02=8:0 70O2=8:0.

#: @0W=0, 61010, <. %0@:V2, 2C;. >@4VT=:V2AL:0, 1.