

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

&"
(PIRACETAM)

!::04:
4VNG0 @5G>28=0: 1 B01;5B:0
4>?>28=8: ;0:B>78 <=>3V4@0B, F5;N;>70 :@8AB0;VG=0, :@>E<0;L ?@565;0B8=V7>20=89,
<03=VN AB50@0B, :@5<=VN 4V>:A84 :>;>W4=89 1572>4=89, B0;L:.

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

\$0@<0:>B5@0?52B8G=0 3@C?0. A8E>AB8@8 B0 ==>B@>?=V 70A>18.
>4 " ! N06B %03.

;V=VG=V E0@0:B5@8AB8:8.
>:070==O.

>@>A;V:
- A8<0B8G=5 ;V:C20==O ?0B>;>3VG=8E AB0=V2, I> AC?@>2>46CNBLAO ?>3V@H5==O< ?0<OBV,
:>3=VB82=8<8 @>7;040<8, 70 28=OB:>< 4V03=>AB>20=>W 45<5=FWW (A;01>C
- ;V:C20==O :>@B8:0;L=>W ;;>=VW O: <=>?@5?0@0B 01> C A;04V :>W B5@0?VW.

@>B8?>:070==O.
=482V4C0;L=0 =5?5@5=>A8EV4=8E ?V@>;V4>=C, 0 B0:>6 V=H8E :>=5=BV2 ?@5?0@0BC.
"5@2>W =54>AB0B=>ABV (?@8 ;V@5=AV :@50B8=V=C<5=H5 20 <;/E2).
>AB@5 ?>@CH5==O <>7:>2>3> :@>2>>1V3C (35<>@03VG=89 V=AC;LB).
%>@5O %0=B8=3B>=0.

!?!>AV1 70AB>AC20==O B0 4>78.
0AB>A>2CNBL ?@5?0@0B ?5@>@0;L=>, 70?820NG8 =525;8:>N :V;L:VABN 2>48.

>@>A;V.
V:C20==O AB0=V2, I> AC?@>2>46CNBLAO ?>3V@H5==O< ?0<OBV, :>3=VB82=8<8 @>7;040<8.
>G0B:>20 4>1>20 4>70 AB0=>28BL 4,8 3 ?@>BO3>< ?5@H>3> B86=O ;V:C20==O. 0728G09 4>7C
@>7?>4V;ONBL =0 2-3 ?@89><8. V4B@870 AB0=>28BL 2,4 3 =0 4>1C, 70 2-3 ?@89><8. # ?>40;LH>1,2 3
=0 4>1C.

V:C20==O :>@B8:0;L=>W ;;>=VW.
>G0B:>20 4>1>20 4>70 AB0=>28BL 24 3 ?@>BO3>< 3 4=V2. /:I> 70 F59 G0A =5 4>AO3=CB> 1060=>3>
B5@0?52B8G=>3> 5D5:BC, ?@>4>26CNBL 70AB>AC20==O ?@5?0@0BC C B>7C20==V (24 3/4>1C) 4>
7 4V1. /:I> =0 7-1C ;V:C20==O =5 >B@8<0=> 1060=>3> B5@0?52B8G=>3> 5D5:BC, ;V:C20==O
?@8?8=ONBL. /:I> B5@0?52B8G=>3> 5D5:BC 1C; > 4>AO3=CB>, B> 7 4=O, :>;8 4>AO3=CB> ABV9:5
?>:@0I5==O, ?>G8=ONBL 7=86C20B8 4>7C ?@5?0@0BC =0 1,2 3 :>6=V 2 4>18 4>B8, 4>:8 7=>2C =5
702;OBLAO ?@>O28 :>@B8:0;L=>W ;;>=VW. &5 40ABL <>6;82VABL 2AB0=>28B8 A5@54=N
5D5:B82=C 4>7C.

>1>2C 4>7C @>7?>4V;ONBL =0 2-3 ?@89><8. V:C20==O V=H8<8 0=B8;;>=VG=8<8 70A>10<8 ?V4B@8
?5@54=L> ?@87=0G5=8E 4>70E. V:C20==O ?@>4>26CNBL 4> 7=8:=5==O A8@N20==O. ;O
?>?5@5465==O ?>3V@H5==O AB0=C E2>@8E =5 <>6=0 @V7:> ?@8?8=OB8 70AB>AC20==O
?@5?0@0BC. 5>1EV4=> ?>ABC?>2> 7=86C20B8 4>7C =0 1,2 3 :>6=V
2-3 4=V. 5>1EV4=> :>6=V 62B>@=V :C@A8 ;V:C20==O ?@5?0@0B><, :>@5:BCNG8 ?@8 FL>7C
70;56=> 2V4 AB0=C ?0FVT=B0, 4> 7=8:=5==O 01> 7<5=H5==O ?@>O2V2 E2>@>18.

0AB>AC20==O ?0FVT=B0< ;VB=L>3> 2V:C.
>@5:FVO 4>78 @5:><5=4CTBLAO ?0FVT=B0< ;VB=L>3> 2V:C 7 4V03=>AB>20=8<8 01> ?V4>7@N20=8
<8 @>7;040<8 DC=:FWW =8@>: (482. @>74V; <>7C20==O E2>@8< 7 ?>@CH5==O< DC=:FWW =8@>:»)).
@8 4>23>B@820;>1EV4=>ABV B0:8< ?0FVT=B0< ?>B@V1=> :>=B@>;N20B8 ;;V@5=A :@50B8=V=C 7
<5B>N 045:20B=>W :>@5:FWW 4>78.
>7C20==O E2>@8< 7 ?>@CH5==O< DC=:FWW =8@>:.

A;V;L:8 ?@5?0@0B 282>48BLAO 7 >@30=V7
1V;LH5==O ?5@V>4C =0?V2282545==O 157?>A5@54=L> ?>2O70=> 7 ?>3V@H5==O< DC=:FVW =8@>:
V :;V@5=AC :@50B8=V=C. &5 B0:>6 AB>ACTBLAO ?0FVT=BV2 ;VB=L>3> 2V:C, C O:8E282545==O
:@50B8=V=C 70;568BL 2V4 2V:C. =B5@20;<0<8 ?>B@V1=> A:>@83C20B8 =0 >A=>2V DC=:FVW
=8@>:.
>7@0EC=>: 4>78 ?@>2>4OBL =0 >A=>2V >FV=:8 ;V@5=AC :@50B8=V=C C ?0FVT=B0 70 D>@N:

[140- 2V: (C @>:0E)] *<0A0 BV;0 (C :3)

:@ = (E 0,85 4;O 6V=>:)

72 * ! :@50B8=V=C C ?;07 (<3/4;)

V:C20==O B0:8< E2>@8< ?@87=0G0NBL 70;56=> 2V4 ABC?5=O B06:>ABV =8@>2>W
=54>AB0B=>ABV, 4>B@8<5=40FV9:

!BC?V=L =8@>2>W =54>AB0B=>ABV	;V@5=A :@50B8=V=C (<; /E2)	>7C20==O
>@<0;L=0 DC=:FVO =8@>:	> 80	28G09=0 4>70, @>74V;5=0 =0 2 01> 4 ?@89><8
53:89	50-79	2/3 728G09=>W 4>78 70 2-3 ?@89> <8
>	30-49	1/3 728G09=>W 4>78 70 2 ?@89><8
"O6:89	< 30	1/6 728G09=>W 4>78 >4=>@07>2>
"5@	-	@>B8?>:070=>

>7C20==O E2>@8< 7 ?>@CH5==O< DC=:FVW ?5GV=:8.
>@83C20==O 4>78 =5 ?>B@V1=5 BV;L:8 4;O E2>@8E 7 ?>@CH5==O< DC=:FVW ?5GV=:8. # @07V
4V03=>AB>20=8E 01> ?V4>7@N20=8E @>7;04V2 DC=:FVW ?5GV=:8 B0 =8@>: :>@5:FVN 4>78
?@>2>4OBL B0:, O: 2:070=> C @>74V;V <>7C20==O E2>@8< 7 ?>@CH5==O< DC=:FVW =8@>:».

>1VG=V @50:FVW.
'0AB>B0 287=0G0TBLAO B0:8< G8=> 4C65 G0AB> (≥ 1/10), G0AB> (≥ 1/100 <1/10), =5G0AB>
(≥ 1/1000 <1/100), @V4:> (≥ 1/10 000 <1/1000), 4C65 @V4:> (<1/10000), ?>>48=>:V 28?04:8 (=5>6;82>
>FV=8B8 G0AB>BC =0 >A=>2V 4>ABC?=8E 40=8E).
I>:C :@>2V B0 ;V
>>48=>:V 28?04:8: 35<>@03VG=V @>7;048.
I>:C VW A8AB5<8.
>>48=>:V 28?04:8: 3V?5@GCB;82VABL, 0=0DV;0:B>W4=V @50:FVW.
A8EVG=V @>7;048.
'0AB>: 7=5@2>20=VABL.
5G0AB>: 45?@5AVO.
>>48=>:V 28?04:8: ?V428I5=0 71C46C20=VABL, B@82>6=VABL, 715=B565==O, 30;NF8=0FVW.
I>:C =5@2>2>W A8AB5<8.
'0AB>: 3V?5@:V=57VO.
5G0AB>: A>;82VABL.
>>48=>:V 28?04:8: 0B0:AVO, ?>@CH5==O @V2=>2038, ?V428I5==O G0AB>B8 =0?04V2 5?V;5?AVW,
3>;>2=89 1V;L, 157A>==O, B@5
I>:C >@30=V2 A;CEC B0 ;01V@8=BC.
>>48=>:V 28?04:8: 70?0<>@>G5==O.
I>:C B@02=>W A8AB5<8.
>>48=>:V 28?04:8: 014>B0, 4V0@5O, =C4>B0, 1;N20==O.
I>:C H:V@8 B0 ?V4H:V@=8E B:0=8=
>>48=>:V 28?04:8: 0=3V>=52@>B8G=89 =01@O:, 45@<0B8B8, 28A8?0==O, :@>?82O=:0, A25@1V6.
I>:C @5?@>4C:B82=>W A8AB5<8.
>>48=>:V 28?04:8: ?V428I5==O A5:AC0;L=>W 0:B82=>ABV.
>A;V465==O.
'0AB>: 71V;LH5==O <0A8 BV;0.
V=HV.

5G0ABV: 0AB5=VO.

5@54>7C20==O.

!8<8: ?>A8;5==O ?@>O2V2 ?>1VG=>W 4VW ?@5?0@0BC. !8<8 ?5@54>7C20==O A?>AB5@V30;8AO
?@8 ?5@>@0;L=>AC20==O ?@5?0@0BC C 4>7V 75 3.
V:C20==O A8<0B8G=5: ?@><820==O H;C=:0, 28;:8:0B8 1;N20==O. !?5F8DVG=>3> 0=B84>BC =5<0T,
<>6=0 70AB>A>2C20B8 35<>4V0;V7 (282545==O 50-60 % ?V@0F5B0

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

5 70AB>A>2C20B8 ?@5?0@0B C ?5@V>4 203VB=>ABV. V@0F5B0< ?@>=8:0T C 3@C4=5 <>;>:, B>
1EV4=>ABV 70AB>A>2C20==O ?@5?0@0BC 3>4C20==O 3@C44N A;V4 ?@8?8=8B8.

VB8.

5 70AB>A>2C20B8.

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

?;82 =0 03@530FVN B@><1>F8BV2.

7207:C 7 B8<, I> ?V@0F5B0< 7=86CT 03@530FVN B@><1>F8BV2 (482. @>74V; «\$0@<0>;>3VG=V
2;0AB82>ABV»), =5>1EV4=> 7 >15@56=VABN ?@87=0G0B8 ?@5?0@0B E2>@8< 7 ?>@CH5==O< 35
<>AB07C, AB0=0<8, I> <>6CBL AC?@>2>46C20B8AL :@>2>28;820<8 (28@07:0 H;C=:>2>-.8H:>2>3>
B@0:BC), ?V4 G0A 7=0G=8E EV@C@3VG=8E >?5@0FV9 (2;:NG0NG8 AB<0B>;>3VG=V
2B@CG0==O), E2>@8< V7 A8<0<8 BO6:>W :@>2>B5GV 01> E2>@8<, O:V <0NBL 2 0=0<=57V 35
<>@03VG=89 V=AC;LB; ?0FVT=B0<, O:V 70AB>A>2CNBL 0=B8:>03C;O=B8, B@><1>F8B0@=V
0=B803@530=B8, 2;:NG0NG8 =87L:V 4>78 0F5B8;A0;VF8;>2>W :8A;>B8. @5?0@0B 282>48BLAO =8@:0
<8, B>1EV4=> >A>1;82C C203C ?@84V;OB8 E2>@8< 7 =8@:>2>N =54>AB0B=VABN.

0FVT=B8 ;VB=L>3> 2V:C.

@8 4>23>B@820;V9 B5@0?VW C E2>@8E ;VB=L>3> 2V:C @5:><5=4CTBLAO @53C;O@=89 :>=B@>;L
?>:07=8:V2 DC=:FVW =8@>:, 70 =5>1EV4=>ABV :>@83CNBL 4>7C 70;56=> 2V4 @57C;LB0BV2
4>A;V465==O ;V@5=AC :@50B8=V=C (482. @>74V; «!>AV1 70AB>AC20==O B0 4>78»).

5@5@820==O 70AB>AC20==O.

@8 ;V:C20==V E2>@8E =0 :>@B8:0;L=C ;>=VN A;V4 C=8:0B8 @V7:>3> ?5@5@820==O ;V:C20==O C
7207:C V7 703@>7>N 35=5@0;V70FVW ;>=VW 01> 28=8:=5==O AC4>

>?5@5465==O, ?>2070=V V7 2< 4>?>28=.

@5?0@0B 7C. ">

**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 7 >15@56=VABN 70AB>A>2C20B8 ?@5?0@0B ?V4 G0A :5@C20==O B@0=A?>@B=8<8 70A>10<8
V @>1>B8 7 V=H8<8 <5E0=V7<0<8, 72060NG8 =0 <>6;82VABL 28=8:=5==O ?>1VG=8E @50:FV9 7 1>:C
F5=B@0;L=>W =5@2>2>W A8AB5<8.

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

@8 ACAC20==V 7 B8@5>W4=8<8 3>@<>=0<8 ("3+"4) <>6;820 ?V428I5=0 4@0BV2;82VABL,
457>@VT=B0FVO V ?>@CH5==O A=C. 5 2V47=0G5=> 270T<>4VW 7 ;>=075?0<><, D5=VB>W=><,
D5=>10@1VB0;><, 20;L?@>0B>< =0B@VN. 8A>:V 4>78 (9,6 3/4>1C) ?V@0F5B0:C<0@>;C C E2>@8E =0
25=>7=89 B@><1>7: A?>AB5@V30;>AO 7=0G=5 7=865==O @V2=O 03@530FVW B@><1>F8BV2,
@V2=O DV1@8=>35=C, D0:B>@V2 V;;V1@0=4B0, 207:>ABV :@>2V V ?;07<8. <>2V@=VABL 71V2
=87L:0, >A:V;L:8 90 % ?@5?0@0BC 282>48BLAO C =57In vitro ?V@0F5B0< =5 ?@83=VGCT F8B>E@><
450 V7>D>@<8 CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1 i 4A9/11 C :>=F5=B@0FVW 142, 426, 1422 CYP
26 (21 %) V 34/5 (11 %). 4=0: @V25=L_V F8E 42>E CYP-V7><5@V2 4>AB0B=V9 ?@8 ?5@528I5==V 1422
7V 20 <3/4>1C =5 7 ?V: V :@82C @V2=O :>=F5=B@0FVW ?@>B85?V;5?B8G=8E ?@5?0@0BV2 C
A8@>20BFV :@>2V (:0@10<075?V=, D5=VB>W=, D5=>10@1VB0;; 20;L?@>0B) C E2>@8E =0
5?V;5?AVN. !C< 7 0;:>3>;5< =5 2?;8202 =0 @V25=L :>=F5=B@0FVW ?V@0F5B020BFV :@>2V V
:>=F5=B@0FVO 0;:>3>;N 2 A8@>20BFV :@>2V =5 7AC20==V 1,6 3 ?V@0F5B0

\$0@<0:>;>3VG=V 2;0AB82>ABV.
\$0@<0:>48=0
:B82=8< :>=5=B>< ?@5?0@0BC T ?V@0F5B0<, F8;;VG=5 ?>EV4=5 30<<0-0<0A;O=>W :8A;>B8.
V@0F5B0< T =>>B@>?=8< 70A>1><, I> 4VT =0 <>7>;, ?>:@0ICNG8 :>3=VB82=V DC=:FVW, B0:V O:
740B=VABL 4> =02G0==O, ?0<'OBL, C2030, 0 B0:>6 @>7C<>2C ?@0F5740B=VABL. 5E0=V72C A8AB5
ABV ?>H8@5==O 71C465==O C 3>;>2=>F8@:C;OFVW H;OE< 2?;82C =0 @5>;>3VG=V
E0@0:B5@8AB8:8 :@>2V, ?@8 FL>@>7H8@N20;L=0 4VO 2V4ACB=O. >:@0ICT 72O7:8 9,6 3 7=86CT
@V25=L DV1@8=>35=C V D0:B>@V2 V;;V1@0=4B0 =0 30-40 % B0 ?>4>26CT G0A :@>2>B5GV.
V@0F5B0< G8=8BL ?@>B5:B>@=C B0 2V4=>2;N20;L=C 4VW ?@8 ?>@CH5==V DC=:FVW 3>;>2=>3>
<>7:C 2=0A;V4>: 3V?>:AVW B0 V=B>:A8:0FVW, 5;5:B@>:>=2C;LA82=>W B5@0?VW. V@0F5B0
7=86CT 28@065=VABL V B@820;VABL 25AB81C;O@=>3> =VAB03>=VW.
\$0@<0:>:V=5B8:0.
(284:> 2A<>:BCTBLAO 7 B@02=>3> B@0:BC V G5@57 30-40 E28;8= 4>AO30T <0:A8<0;L=>W
:>=F5=B@0FVW 2 :@>2V. >1@5 ?@>=8:0T :@V7L 35<0B>5=F8D0;VG=89 V ?;0F5=B0@=89 10@T@8. #
<>7:>2V9 B:0=8=V =0:>?8GCTBLAO G5@57 1-4 3>48=8. 5@V>4 =0?V2282545==O AB0=>28BL
?@81;87=> 4 3>48=8. V A?8==<>7:>2>W @V48=8 282>48BLAO 7=0G=> ?>2V;L=VH5, I> A2V4G8BL
?@> 28A>:89 B@>?V7< 4> <>7:>2>W B:0=8=8. @0:B8G=> =5 <5B01>;V7CTBLAO. 90 % 284V;OTBLAO
=8@:0<8 C =57

\$0@<0F52B8G=V 2;0AB82>ABV.
>A=>2=V DV78:>-EVABV: B01;5B:8 1V;>3> 7 :@52VABL.

"5@ABV. 2 @>:8.
5 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 ACE>!. 15@V30B8 C =54>ABC?=>

#?0:>2:0.
> 10 B01;5B>: C 1;VAB5@V, ?> 6 1;VAB5@V2 C ?0GFV 7 :0@B>=C.

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

8@>1=8:..
" «%V

VAF57=0E>465==O.
61010, #: @0W=0, @4VT=:V2AL:0, 1.