

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

"□ !□®  
(TOMOHEXOL)

!;:04:

4VNG0 @5G>28=0: iohexol;

1 <; @>7G8=C 35:A>;C 2 ?5@5@0EC20==V =0 100 % @5G>28=C, I> 5:2V20;5=B=> 9>4C:

<3 9>4C/<;	240	300	350
<3 9>35:A>;C/<;	518	647	755

4>?>28=8: =0B@VN :0;LFDVN 545B0B, B@><5B0B0 E;>@8AB>2>4=520 @>72545=0,

2>40 4;O V=T: FV9.

V:0@AL:0 D>@<0. >7G8= 4;O V=T: FV9.

\$0@<0:>B5@0?52B8G=0 3@C?0. >4>2:>=B@0AB=V 70A>18. >4>@>7G8==V =87L:>>A<>;O@=V

=5D@>B@>?>V @5=B35=>:>=B@0AB=V 70A>18. >4 " ! V08A B02.

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

>:070==O.

"><>35:A>;® ?@87=0G5=89 BV;L:8 4;O 4V03=>AB8G=8E FV;59.

5=B35=>:>=B@0AB=89 ?@5?0@0B 4;O 70AB>AC20==O 4VBO< B0 4>@>A;8< 7 <5B>N ?@>2545==O

:0@4V>0=3V>3@0DVW, 0@B5@V>3@0DVW, C@>3@0DVW, D;51>3@0DVW V :>=B@0AB=>3>

?>A8;5==O ?@8 :><>3@0DVW ("); ?@8 ?>?5@5:>2V9, 3@C4=V9 B0 H89=V9 3@0DVW, "-

F8AB5@=>3@0DVW ?VA;O AC10@0E=>W40;L=>3> 22545==O; 0@B@>3@0DVW, 5=4>A:>?VG=V9

@5B@>3@04=V9 ?0=:@50B>3@0DVW (), 5=4>A:>?VG=V9 @5B@>3@04=V9

E>;0=3V>?0=:@50B>3@0DVW (%), 35@=V>3@0DVW, 3VAB5@>A0;L?V=3>3@0DVW, AV0;>3@0DVW

B0 4>A;V465==OE H;C=:>2>-:8H:>2>3> B@0:BC.

@>B8?>:070==O.

V428I5=0 GCB;82VABL 4> 9>4C 01>4> V=H8E :>=5=BV2 ?@5?0@0BC. 8@065=89 B8@5>B>:A8:>7.

?V;5?AVO B0 F5@51@0;L=V V=D5:FVW (4;O AC10@0E=>W40;L=>3> 22545==O).

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

;O 2=CB@VH=L>0@B5@V0;L=>3>, 2=CB@VH=L>25==>3>, V=B@0B5:0;L=>3>,

2=CB@VH=L>?>@>6=8==>3> 22545==O, ?5@>@0;L=>3> ?@89>3> 22545==O 4>@>A;8< V 4VBO

>70 ?@5?0@0BC 70;568BL 2V4 <5B>4C 4>A;V465==O, 2V:C, <0A8 BV;0, E28;8==>3> >1 T3> AB0=C

?0FVT=B0 B0 B5E=V:8 70AB>AC20==O ?@5?0@0BC. 5@54 B0 ?VA;O 70AB>AC20==O :>=B@0AB=>W

@5G>28=8, B0: O: V 4;O V=H8E @5=B35=>:>=B@0AB=8E 70A>1V2, =5>1EV4=> 70157?5G8B8

2V4?>2V4=C 3V4@0B0FVN >@30=V7

>:070==O	>=F5=B@0FVO 1'T< 9>4C, <3/<;	?@5?0@0BC, <;	A>1;82V 2:07V2:8
=CB@VH=L>25==5 22545==O			
#@>3@0DVO			
>@>A;V	300 01> 350	40-80	>:@5<8E 28?04:0E <>6;825 22545==O 1V;LH5 80 <;
VB8 (<0A0 BV;0 <5=H5 7 :3)	240 300	4 <:/:3 3 <:/:3	
VB8 (<0A0 BV;0 1V;LH5 7 :3)	240 300	3 <:/:3 2 <:/:3	<0:A. 4>70 40 <;
\$;51>3@0DVO (=86=V :V=FV2:8)	240 01> 300	20-100 (=0 >4=C :V=FV2:C)	
&8D@>20 AC1B@0:FV9=0 0=3V>3@0DVO	300 01> 350	20-60	

<b>&gt;A8;5==O ?@8 "</b>			
>@>A;V	240	100-250	030;L=0 :V;L:VABL 9>4C 2 V= T:FVW 70728G09 AB0=>28BL 30-60 3
	300	100-200	
	350	100-150	
VB8	240	2-3 <:/:3 (4> 40 <);	>:@5<8E 28?04:0E <>6;825 22545==O 4> 100 <;
	300	1-3 <:/:3 (4> 40 <);	
<b>=CB@VH=L&gt;0@B5@V0;L=5 22545==O</b>			
<b>@B5@V&gt;3@0DVO:</b>			
4C30 0>@B8	300	30-40	1□T< =0 >4=C V=T:FVN 70;568BL 2V4
A5;5:B82=0 F5@51@0;L=0 0=3V>3@0DVO	300	5-10	
0>@B>3@0DVO	350	40-60	
0=3V>3@0DVO AB53=>28E 0@B5@V9	300 01> 350	30-50	
V=HV 2848	300	70;568BL 2V4 <5B>4C 4>A;V465==O	
<b>0@4V&gt;0=3V&gt;3@0DVO:</b>			
>@>A;V ;V289 H;C=>G>;. :>@V=L 0>@B8, A5;5:B82=0 :>@>=0@>3@0DVO	350	30-60	
	350	4-8	
VB8	300 01> 350	>70 70;568BL 2V4 2V:C, <0A8 BV;0 B0 70E2>@N20==O	<0:A. 4>70 8 <:/:3
<b>&amp;8D@&gt;20 ACIB@0:FV9=0 0=3V&gt;3@0DVO</b>	240 01> 300	1-15	0;56=> 2V4 1CB8 28:>@8AB0=V >1T<8 4> 30 <;
<b>=B@0B5:0;L=5 22545==O</b>			
<b>&gt;?5@5:&gt;20 B0 3@C4=0 3@0DVO</b>	240	10-15	;N<10;L=5 22545==O
		8-12	
<b>(89=0 3@0DVO</b>	240	10-12	;N<10;L=5 22545==O
	300	7-10	
	240	6-10	1>:>25 H89=5 22545==O
	300	6-8	
<b>" F8AB5@=&gt;3@0DVO</b>	240	4-12	;N<10;L=5 22545==O
<b>=CB@VH=L&gt;?&gt;@&gt;6=8==5 22545==O</b>			
<b>@B@&gt;3@0DVO</b>	240	5-20	
	300	5-15	
	350	5-10	
/%	240	20-50	
<b>5@=V&gt;3@0DVO</b>	240	50	1□T< 22545==O 70;568BL 2V4 >1T 3@86V
<b>VAB5@&gt;A0;L?V=3&gt;3@0DVO</b>	240	15-50	
	300	15-25	
<b>!V0;&gt;3@0DVO</b>	240 01> 300	0,5-2	
<b>5@&gt;@0;L=5 70AB&gt;AC20==O</b>			

<b>&gt;A;V465==O ("</b>			
>@>A;V	350	87=0G0TBLAO V=482V4C0;L=>	
VB8 (AB@02>EV4)	300 01> 350	2-4 <:/:3	0:A8<0;L=0 4>70 50 <;
54>=>H5=V 4VB8	350	2-4 <:/:3	
<b>&gt;A8;5==O ?@8 "</b>			
>@>A;V	>725AB8 2>4>N 4> :=F5=B@0FVW 1;87L:> 6 <3 9>4C/<;	800-2000 <; >B@8 <0=>3> @>7G8=C ?@>BO3<< 287=0G5=>3> ?5@V>4C 15-20 <; >B@8 <0=>3> @>7G8=C/:3 <0A8 BV;0	0?@8:;04: @>725AB8 "><< 35:A>;@-300 01> "><<35:A>;@- 350 2>4>N 1:50
VB8			
<b>5:B0;L=5 22545==O</b>			
>A8;5==O ?@8 " VB8	>725AB8 2>4>N 4> :=F5=B@0FVW 1;87L:> 6 <3 9>4C/<;	87=0G0TBLAO V=482V4C0;L=>	0?@8:;04: @>725AB8 "><< 35:A>;@-300 01> "><<35:A>;@- 350 2>4>N 1:50
>A;V465==O (" VB8	240 01> 300, 01> 350 @>725AB8 2>4>N 4> :=F5=B@0FVW 100150 <3 9>4C/<;	5□10 <:/:3 >B@8 <0=>3> @>7G8=C	0?@8:;04: @>725AB8 "><< 35:A>;@-240, "><<35:A>;@-300 01> "><<35:A>;@-350 2>4>N 1:1 01> 1:2

**>1VG=V @50:FVW.**

030;L=V 2848 ?>1VG=8E @50:FV9 (E0@0:B5@=V 4;O 2AVE 9>4>2:=B@0AB=8E 70A>1V2). 86G5  
?@82545=V <>6;82V >A=>2=V ?>1VG=V 5D5:B8, I> ?>2O70=V 7 ?@>2545==O< @5=B35=>;>3VG=8E  
?@>F54C@ V7 70AB>AC20==O< =5V>==8E :=B@0AB=8E 70A>1V2.  
50:FVW 3V?5@GCB;82>ABV <>6CBL 28=8:0B8 =570;56=> 2V4 4>78 ?@5?0@0BC, I> 22>48BLAO, V  
A?>A>1C 22545==O. 53:V A8<8 <>6CBL 1CB8 ?5@H8<8 >7=0:0<8 A5@9>7=>W 0=0DV;0:B8G=>W  
@50:FVW/H>:C. 2545==O :=B@0AB=>W @5G>28=8 A;V4 =5309=> ?@8?8=8B8 B0 C @07V  
=5>1EV4=>ABV ?@>25AB8 A?5F8DVG=C B5@0?VN V7 2=CB@VH=L>AC48==8< 22545==O< ;V:V2.  
"@0=78B>@=5 ?V428I5==O S:@50B8=V=C T G0AB8< O28I5< ?VA;O 70AB>AC20==O 9>4>2  
:=B@0AB=8E 70A>1V2, ?V428ICTBLAO @878: 28=8:=5==O :=B@0ABV=4C:>20=>W =5D@>?0BVW.  
>487< 01> 9>4=89 ?0@>B8B 4C65 @V4:VA=0 @50:FVO =0 22545==O 9>4>2:=B@0AB=8E 70A>1V2.  
>=0 <>65 28@060B8AO C 283;O4V =01@O:C B0 1>;N C A;8==8E 70;>70E ?@>BO3<< 10 4=V2 ?VA;O  
4>A;V465==O.

I>:C VW A8AB5<8: @50:FVW 3V?5@GCB;82>ABV (2;;NG0NG8 7048H:C, 28A8?, 5@8B5?82O=:C,  
A25@1V6, H:V@=V @50:FVW, 20A:C;VB, 0=3V>=52@>B8G=89 =01@O:, =01@O: 3>@B0=V,  
;0@8=3>A?07<, 1@>=E>A?07< 01> =5:0@4V>35==89 =01@O: ;535=L <>6CBL @>72820B8AO O:  
157?>A5@54=L> ?VA;O 22545==O ?@5?0@0BC, B0: V G5@57 45:V;L:0 4=V2),0=0DV;0:B8G=V  
/0=0DV;0:B>W4=V @50:FVW, 0=0DV;0:B8G=89/0=0DV;0:B>W4=89 H>:.

I>:C =5@2>2>W A8AB5<8: 3>;>2=89 1V;L, 48A3527VO (<8=CI89 <5B0;5289 ?@8A<0:), 207>2030;L=0  
=5?@8B><=VABL.

I>:C A5@F52>-AC48==>W A8AB5<8: 1@048:0@4VO, 0@B5@V0;L=0 3V?5@B5=7VO, 0@B5@V0;L=0 3V?>B5=7VO.  
I>:C B@02=>W A8AB5<8: =C4>B0, 1;N20==O, 4V0@5O, 1V;L/48A:>@B 2 5?V30AB@0;L=V9 4V;O=FV, 71V;LH5==O @>77.  
030;L=V @>7;048: 2V4GCBBO 60@C, ?V@5:AVO, B@57=>1).  
"@02<8, >B@CT==O VCA.;04=5==O ?@>F54C@: 9>487  
>1VG=V @50:FVW, ?>2O70=V V7 2=CB@VH=L>AC48==8< (2=CB@VH=L>0@B5@V0;L=8< B0 2=CB@VH=L>25==8<) 22545==O  
>728B>: ?>1VG=8E @50:FV9, I> <>6CBL A?>AB5@V30B8AL ?V4 G0A 2=CB@VH=L>0@B5@V0;L=>3> 22545==O, 70;568BL 2V4 @8 A5;5:B82=V9 0=3V>3@0DVW B0 V=H8E 4>A;V465==OE, :>;8 :>=B@0AB=89 70AV1 C 28A>:V9 :>=F5=B@0FVW ?@>=8:0T 4> >@30=C, I> 4>A;V46CTBLAO, <>6CBL A?>AB5@V30B8AO ?>@CH5==O DC=:FV9 40=>3> >@30=C.  
I>:C VW A8AB5<8: @50:FVW 3V?5@GCB;82>ABV, 2;;NG0NG8 =5157?5G=C 4;O 68BBO 01> ;5B0;L=C 0=0DV;0:AVN, BO6:V ?CABC;L>7=V, 5:AD>;V0B82=V 01> 1C;L>7=V @50:FVW.  
I>:C 5=4>:@8==>W A8AB5<8: B8@5>B>:A8:>7, B@0=78B>@=89 3V?>B8@5>W487  
I>:C ?A8EV:8: A?;CB0=VABL A2V4<>>ABV.  
I>:C =5@2>2>W A8AB5<8: 70?0<>@>G5==O, AC4<8, ?>@CH5==O A2V4<>>ABV, 5=F5D0;>?0BVO, ABC?>@, @>7;048 GCB;82>ABV (2;;NG0NG8 3V?5AB57VN), ?0@5AB57VO, B@5<>@, 3>;>2=89 1V;L, 48A3527VO, B@0=78B>@=0 <>B>@=0 48ADC=:FVO (2;;NG0NG8 <>2=V @>7;048, 0D07VN, 4870@B@VN), B@0=78B>@=0 :>=B@0AB=0 5=F5D0;>?0BVO (2;;NG0NG8 B@0=78B>@=C 352C 2B@0BC ?0<OBV, 457>@VT=B0FVN, :>3@04=C 0<=57VN).  
I>:C >@30=V2 7>@C: B@0=78B>@=0 :>@:>20 A;V?>B0.  
I>:C >@30=V2 A;CEC B0 @V2=>2038: B@0=78B>@=0 2B@0B0 A;CEC.  
I>:C A5@F52>-AC48==>W A8AB5<8: 0@8B:0@40, 3V?5@5:C A5@FO (2;;NG0NG8 7C?8=:C A5@FO, :0@4V>@5A?V@0B>@=C 7C?8=:C), A?07< :>@>=0@=8E 0@B5@V9, 1V;L C 3@C4OE, H>;, 0@B5@V0;L=89 A?07<, VH5<1>D;51VB B0 B@<>1>7.  
I>:C 48E0;L=>W A8AB5<8: :0H5;L, 48A?=>5, =5:0@4V>35==89 =01@O: ;535=V2, 3>AB@V @5A?V@0B>@=V A8<8, 1@>=E>A?07<, ;0@8=3>A?07<, =0?04 0AB<8.  
I>:C B@02=>W A8AB5<8: 4V0@5O, =C4>B0, 1;N20==O, 71V;LH5==O A;8==8E 70;>7, 1V;L C 682>BV, 703>AB@5==O ?0=:@50B8BC, 3>AB@89 ?0=:@50B8B.  
I>:C H:V@8 B0 ?V4H:V@=8E B:0=8=: @<=0 5@8B5<0, 3>AB@89 35=5@0;V7>20=89 5:70=B5<0B>7=89 ?CABC;L>7, 1C;L>7=89 45@<0B8B, A8=4@< !BV25=A0-6>=A>=0, B>:A8G=89 5?V45@<0;L=89 =5:@>;V7, <548:0<5=B>7=0 H:V@=0 @50:FVO, I> AC?@>2>46CTBLAO 5>78=>DV;VTN B0 A8AB5<=8 <8 ?@>O20<8, @0?B>25 703>AB@5==O ?A>@V07C.  
I>:C >?>@=>-@CE>2>3> 0?0@0BC B0 A?>;CG=>W B:0=8=8: 0@B@0;3VO.  
I>:C =8@>: B0 A5G>282V4=8E H;OEV2: ?>@CH5==O DC=:FV9 =8@>;, 2;;NG0NG8 3>AB@C =8@:>2C =54>AB0B=VABL.  
030;L=V @>7;048 B0 72V4GCBBO 60@C, 1V;L B0 48A:>@B, 0AB5=VG=89 AB0= (2;;NG0NG8 =574C60==O, 2B>7=>1), 3V?5@B5@ =B@0B5:0;L=5 22545==O.  
>1VG=V @50:FVW <>6CBL 28=8:0B8 G5@57 45:V;L:0 3>48= 01> 4=V2 ?VA;O V=B@0B5:0;L=>3> 22545==O. E G0AB>B0 ?@81;87=> 2V4?>2V40T G0AB>BV CA.;04=5=L ?VA;O ;N<10;L=8E ?C=:FV9 157 22545==O :>=B@0AB=>3> 70A>1C. ;O B>3>, I>1 1V30B8 =04A?8==><>7:>2>W @V48=8.  
I>:C VW A8AB5<8: @50:FVW 3V?5@GCB;82>ABV, 2;;NG0NG8 0=0DV;0:B8G=V/0=0DV;0:B>W4=V @50:FVW.  
I>:C ?A8EV:8: A?;CB0=VABL A2V4<>>ABV.  
I>:C =5@2>2>W A8AB5<8: 3>;>2=89 1V;L (<>65 1CB8 A8;L=8< B0 B@820;8<), 0A5?B8G=89 <5=V=3VB (2;;NG0NG8 EVAC4<>8, 70?0<>@>G5==O, 48A3527VO, 207>2030;L=5 A8=:>?5, ?>@CH5==O @8B3@0 <8, <5=V=3V7<, B@0=78B>@=0 :>=B@0AB=0 5=F5D0;>?0BVO (2;;NG0NG8 B@0=78B>@=C 35 B82C 2B@0BC ?0<OBV, :>@, @5B@>3@04=C 0<=57VN), B@0=78B>@=0 <>B>@=0 48ADC=:FVO (2;;NG0NG8 <>2=V @>7;048, 0D07VN, 4870@B@VN), ?0@5AB57VO, 3V?5AB57VO, @>7;048 GCB;82>ABV.  
I>:C >@30=V2 7>@C: B@0=78B>@=0 :>@:>20 A;V?>B0, A2VB;>1>O7=L.  
I>:C >@30=V2 A;CEC B0 @V2=>2038: B@0=78B>@=0 2B@0B0 A;CEC.  
I>:C B@02=>W A8AB5<8: 1V;L C 682>BV, 71V;LH5==O A;8==8E 70;>7, =C4>B0, 1;N20==O, 4V0@5O.

I>:C >?>@=>-@CE>2>3> 0?0@0BC B0 A?>;CG=>W B:0=8=8: 1V;L C H8W, 1V;L C A?8=V, A?078.  
030;L=V @>7;048 B0 71V;L C :V=V2:0E, 2V4GCBBO 60@C, ?V@5:AVO, B@57=>1), 7  
>1VG=V @50:FVW, ?>2O70=V 7 2=CB@VH=L>?>@>6=8==8< 22545==O

I>:C VW A8AB5<8: @50:FVW 3V?5@GCB;82>ABV, 2;;NG0NG8 0=0DV;0:B8G=V/0=0DV;0:B>W4=V  
@50:FVW.

I>:C =5@2>2>W A8AB5<8: 3>;>2=89 1V;L, 48A3527VO, 207>2030;L=5 A8=>?5.

I>:C B@02=>W A8AB5<8: =C4>B0, 1V;L C 682>BV,71V;LH5==O A;8==8E 70;>7, 1;N20==O, 4V0@50;  
?@8 3VAB5@>A0;L?V=3>3@0DVW 1V;L 2=87C 682>B0.

030;L=V @>7;048 B0 72V4GCBBO 60@C, ?V@5:AVO, B@57=>1).

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

I>:C B@02=>W A8AB5<8: 4V0@50, =C4>B0, 1;N20==O, 1V;L C 682>BV.

VAB5@>A0;L?V=3>3@0DVO (!).

I>:C B@02=>W A8AB5<8: 1V;L C =86=VE 2V44V;0E 682>B0.

@B@>3@0DVO.

I>:C >?>@=>-@CE>2>3> 0?0@0BC B0 A?>;CG=>W B:0=8=8: 0@B@8B.

030;L=V @>7;048 B0 ?>@CH5==O C : 1V;L.

:@51VG=V @50:FVW.

>2V4><;O;>AO ?@> @>728B>: B@><1>5<1>;VG=8E CA;;04=5=L C 72 07:C 7 ?@>2545==O<

:>=B@0AB=>W 0=3V>3@0DVW :>@>=0@=8E, <7:>28E, =8@:>28E B0 ?5@8D5@8G=8E 0@B5@V9.

>=B@0AB=0 @5G>28=0 <65 A?@8OB8 @>728B:C CA;;04=5=L (482. @>74V; «A>1;82>ABV

70AB>AC20==O»). >2V4><;O;>AO ?@> @>728B>: CA;;04=5=L 7 1>:C A5@FO, 2;;NG0NG8 3>AB@89

V=D0@:B :0@40 ?V4 G0A 01> ?VA;O ?@>2545==O :>=B@0AB=>W :>@>=0@=>W 0=3V>3@0DVW.

0FVT=B8 ;VB=L>3> 2V:C 01> ?0FVT=B8 7 BO6:>N VH5N E2>@>1>N A5@FO, =5AB01V;L=>N

AB5=>:0@4VTN B0 48ADC=:FVTN ;V2>3> H;C=>G:0 <0;8 28I89 @878: @>728B:C CA;;04=5=L (482.

@>74V; «A>1;82>ABV 70AB>AC20==O»).

# ?>>48=>:8E 28?04:0E :>=B@0AB=89 70AV1 <65 ?@>=8:0B8 G5@57 35<0B>5=F5D0;VG=89 10@T@, C

@57C;LB0BV G>3> 28=8:0T =0:>?8G5==O ?@5?0@0BC 2 :>@V 3>;>2=>3> <7:C, I> <65 A?@8G8=8B8

=52@>;>3VG=V @50:FVW, 2;;NG0NG8 AC4<8, B@0=78B>@=V <B>@=V 01> A5=A>@=V @>7;048,

B@0=78B>@=5 ?>@CH5==O A2V4<>ABV, B@0=78B>@=C 2B@0BC ?0<OBV B0 5=F5D0;>?0BVN

(482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

=0DV;0:B>W4=V @50:FVW B0 0=0DV;0:B>W4=89 H>:<65 ?@8725AB8 4> 3;81>:>W 3V?>B5=7VW B0

?>2O70=8E 7 =5N A8:A8G=C 5=F5D0;>?0BVN, =8@:>2C B0 ?5GV=:>2C =54>AB0B=VABL (482. @>74V;

«A>1;82>ABV 70AB>AC20==O»).

45O:8E 28?04:0E B@0=AAC40FVO :>=B@0AB=>W @5G>28=8 A?@8G8=OT ;>:0;L=89 1V;L B0 =01@O;.

O:V 70728G09 ?@>E>4OBL 157 CA;;04=5=L. 0DV:A>20=V 28?04:8 70?0;5==O, =5:@>7C B:0=8= V :>(482.

@>74V; «A>1;82>ABV 70AB>AC20==O»).

0FVT=B8 48BOG>3> 2V:C. !;V4 ?0<□OB0B8 ?@> <6;82VABL @>728B:C B@0=78B>@=>3>

3V?>B8@5>W487=>H5=8E, =>2>=0@>465=8E B0 V=H8E 4VB59 C 72O7:C 7 22545==O< 9>4>2

:>=B@0AB=8E @5G>28=.

54=>H5=V 4VB8 <0NBL ?V428I5=C GCB;82VABL 4> 9>4C. >2V4><;O;>AO ?@> @>728B>:

B@0=78B>@=>3> 3V?>B8@5>W487=>H5=8E 4VB59, O:V 7=0E>4OBLAO =0 3@C4=>4>2C20==V.

>35:A>; =5>4=>@07>2> ?@87=0G0;8 6V=:0<, O:V 3>4CNBL 3@C44N (482. @>74V; «A>1;82>ABV

70AB>AC20==O»).

A>1;82> =5<>2;OB0< 4> B0 ?VA;O 22545==O :>=B@0AB=>3> ?@5?0@0BC =5>1EV4=> 70157?5G8B8

045:20B=C 3V4@0B0FVN. V:C20==O =5D@>B>:A8G=>ABV <0T 1CB8 72065=8

0;56=> 2V4 2V:C 7<5=HCTBLAO H284:VABL ;C1>G:>2>W DV;LB@0FVW C =5>2;OB, I> <65

?@8725AB8 4> 70B@8=B@0AB=8E @5G>28=.

5@54>7C20==O.

>;V=VG=V 40=V A2V4G0BL ?@> 25;8:C H8@>BC B5@0?52B8G=>3> 2V:=0 9>35:A>;C B0

2V4ACB=VABL 25@E=L>W <56V AB0=40@B=> ?@8?CAB8<8E 4>7 4;O 2=CB@VH=L>AC48==>3>

70AB>AC20==O. 878: @>728B:C A87C20==O

# @07V ?5@54>7C20==O =5>1EV4=> ?@>25AB8 :>@5:FVN ?>@CH5=L 2>4=>-5;5:B@>;VB=>3>

10;0=AC. 0ABC?>V 3 4=V A;V4 ?@>2>48B8 <=>VB>@8=3 DC=:FV9 =8@>:. # @07V =5>1EV4=>ABV

70AB>AC20B8 35<>4V0;V7 4;O 2840;5==O =04;8H:V2 ?@5?0@0BC. !?5F8DVG=>3> 0=B84>BC =5

VA=CT.

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

03VB=VABL. 57?5:0 70AB>AC20==O ?@5?0@0BC 2 ?5@V>4 203VB=>ABV =5 2AB0=>2;5=0. 57C;LB0B8 5:A?5@8<5=B0;L=8E 4>;V=VG=8E 4>A;V465=L, I> AB>AC20;8AO @5?@>4C:B82=>ABV, @>728B:C 5 <1@V>=0 01> ?;>40, ?5@51V3C 203VB=>ABV, ?5@8- B0 ?>AB=0B0;L=>3> @>728B:C, =5 2:07CNBL =0 VA=C20==O?@O<>3> 01> =5?@O<>3> H:V4;82>3> 2?;82C. > <>6;82>ABV A;V4 C=8:0B8 ?@><5=52>3> 2?;82C C ?5@V>4 203VB=>ABV, =5>1EV4=> 282065=> ?V4V9B8 4> ?@87=0G5==O @5=B35=V2AL:>3> 4>A;V465==O, 7 :>=B@0AB=8< 70A>1><< G8 157 =L>3>, G5@57 <>6;8289 @878:.

"><>35:A>;® C ?5@V>4 203VB=>ABV <>6=0 70AB>A>2C20B8 ;8H5 C @07V =030;L=>W ?>B@518 73V4=> 7 @5:><5=40FVO<8 ;V:0@O B0 ?VA;O @5B5;L=>W >FV=:8 A?V22V4=>H5==O :>@8ABL /@878:.

>4C20==O 3@C44N. >=B@0AB=V 70A>18 =57=0G=>N N ?@>=8:0NBL C 3@C4=5 <>;>: B0 40 <0;>V <>2V@=89.

VA;O 22545==O 9>4>2=B@0AB=8E 70A>1V2 6V=FV, 3>4C20==O 3@C44N <>6=0 ?@>4>26C20B8. # 4>A;V465==V :V;L:VABL 9>35:A>;C, I> 284V;8;0AO 7 3@C4=8< <>;>: <?@>BO3<< ?5@H8E 24 3>48= ?VA;O 22545==O AB0=>28;00,5 % 4>78 7 ?>?@02:>N =0 <0AC BV;0. V;L:VABL 9>35:A>;C, I> ?>B@0?;OT 2 >@30=V7< 48B8=8 ?@>BO3<< ?5@H8E 24 3>48= ?VA;O 22545==O, AB0=>28BL ;8H5 0,2 % 48BOG>W 4>78.

### **VB8.**

@5?0@0B 70AB>A>2CNBL C ?54V0B@8G=V9 ?@0:B8FV.

### **A>1;82V 70E>48 157?5:8.**

/: V 2AV 70A>18 4;O ?0@5=B5@0;L=>3> 22545==O, ?5@54 70AB>AC20==O< ?@5?0@0B "><>35:A>;® A;V4 2V7C0;L=> ?5@52V@8B8 =0 2V4ACB=VABL =5@>7G8==8E G0AB8=>;, 7;L>@C B0 ?>@CH5=L FV;VA=>ABV C?0:>2:8. A:V;L:8 "><>35:A>;® =5 =A5@20=V2, ?@5?0@0B =018@0NBL C H?@8F 157?>A5@54=L> ?5@54 70AB>AC20==O=8 ?@87=0G5=V BV;L:8 4;O >4=>@07>2>3> 70AB>AC20==O. 528:>@8AB0=V 70;8H:8 ?@5?0@0BC ?>B@V1=> 7=818B8.

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

030;L=V >A>1;82>ABV 70AB>AC20==O =5V>==8E <>=><5@=8E :>=B@0AB=8E 70A>1V2. 002=VABL 2 0=0<=57V 0;5@3VW, 0AB<8 B0 =51060=8E @50:FV9 =0 9>4>2=B@0AB=V ?@5?0@0B8 ?>B@51CT ?V428I5=>W C2038. # F8E 28?04:0E =5>1EV4=> @>73;O=CB8 <>6;82VABL ?@5<548:0FVW :>@B8:>AB5@>W40<8 01> 0=B03>=VAB0<8 H1- B0 H2- 3VAB028E @5F5?B>@V2. 878: 28=8:=5==O BO6:8E ?>1VG=8E @50:FV9 =0 "><>35:A>;® 4C65 <0;89. 4=0: 9>4>2=B@0AB=V @5G>28=8 <>6CBL A?@8G8=8B8 703@>7;82V 4;O 68BBO, D0B0;L=V 0=0DV;0:B8G=V/ 0=0DV;0:B>W4=V @50:FVW 01> V=HV ?@>O28 3V?5@GCB;82>ABV. FVTW ?@8G8=8 A;V4 70740;53V4L ?5@5410G8B8 ?>A;V4>2=VABL ;V:C20;L=8E 70E>4V2 C @07V 28=8:=5==O A5@9>7=8E ?>1VG=8E @50:FV9 B0 <0B8 2 =0O2=>ABV =5>1EV4=V ?@5?0@0B8 V >1;04=0==O. 0T 1CB8 ?>ABV9=0 :0=N;O 01> :0B5B5@ =0 G0A ?@>2545==O @5=B35=>:>=B@0AB=>3> 4>A;V465==O 7 <5B>N ?>;53H5==O H284:>3> 2=CB@VH=L>25==>3> 22545==O ;V:0@AL:8E 70A>1V2. # ?0FVT=V2, I> 70AB>A>2CNBL 15B0-04@5=>1;>;0B>@8, ?@>O28 0=0DV;0:AVW<>6CBL 1CB8 0B8?>28<8 V ?><8;>2> 22060B8AO 203CA=8<8 @50:FVO<8. >@V2=O=> 7 V>==8<8 ?@5?0@0B0<8 =5V>==V :>=B@0AB=V 70A>18 <5=H5 2?;820NBL *in vitro* =0 A8AB503C;OFVW :@>2V. @8 ?@>2545==V ?@>F54C@ AC48==>W :0B5B5@870FVW A;V4 4C65 @5B5;L=> 4>B@8<1>7V2 B0 5<1>;V9, I> ?>2O70=V 7 2B@CG0==O 5@54 B0 ?VA;O 22545==O :>=B@0AB=>3> ?@5?0@0BC =5>1EV4=> 70157?5G8B8 045:20B=5 =0A8G5==O >@30=V7A;V46C20=>3> @V48=>N (3V4@0B0FVN). &5 <0T >A>1;825 7=0G5==O 4;O ?0FVT=V2 7 <=>N E2>@>1>N, FC:@>28< 4V015B<<, ?>@CH5==O< DC=:FVW =8@>;, 0 B0:>6 4;O =5 <>2;OB, <0;5=L:8E 4VB59 V ?0FVT=V2 ;VB=L>3> 2V:C. !;V4 1CB8 C206=8< ?@8 4>A;V465==V ?0FVT=V2 7 BO6:8<8 A5@F52>-AC48==8<8 70E2>@N20==O<8 V ;535=52>N 3V?5@B5=7VTN C 7207:C 7 @878:<< @>728B:C 0@8B ?>@CH5=L 35<>48=0

%2>@V 7 3>AB@>N F5@51@0;L=>N ?0B>;>3VTN, ?CE;8=0<8 <>7:C B0 5?V;5?AVTN AE8;L=V 4>  
@>728B:C AC4< V ?>B@51CNBL >A>1;82>W C2038. V428I5=89 @878: @>728B:C AC4< V  
=52@>;>3VG=8E @50:FV9 C 0;:>3>;V:V2 V =0@:<0=V2. V4:> A?>AB5@V30;8AO 28?04:8 B82>W  
2B@0B8 A;CEC 01> 3;CE>B8 ?VA;O3@0DVW, I>, =0?52=>, ?>2O70=> V7 ?04V==O< B8A:C A?8==>  
<>7:>2>W @V48=8 2=0A;V4>: ;N<10;L=>W ?C=:FVW.  
;O 70?>1V30==O @>728B:C :>=B@0ABV=4C:>20=>W =5D@>?0Bvw, ?>@CH5==O DC=:FV9 =8@>:  
01> 3>AB@>W =8@:>2>W =54>AB0B=>ABV, ?>2O70=>W V7 22545==O< :>=B@0AB=>W @5G>28=8,  
=5>1EV4=0 >A>1;820 >15@56=VABL ?@8 4>A;V465==V E2>@8E, O:V 265<0NBL ?>@CH5==O  
DC=:FV9 =8@>:, V E2>@8E =0 FC:@>289 4V015B, O:V =0;560BL 4> 3@C?8 @878:C. "5 6 A0<5  
AB>ACTBLAO V 4>A;V465==O ?0FVT=BV2 7 ?0@0?@>B5W=5<=0 E2>@>10, <0:@>3;>1C;V=5  
=B@0AB=V 70A>18 E2>@8< =0 D5>E@><>F8B> ?0FVT=B0<, O:V =0;560BL 4> 3@C?8 @878:C.  
0E>48 I>4> 70?>1V30==O ?>1VG=8< @50:FVO  
2AB0=>2;5==O ?0FVT=BV2, O:V =0;560BL 4> 3@C?8 @878:C;  
70157?5G5==O 045:20B=>W 3V4@0B0FVW; O:I> =5>1EV4=>, F5 <>65 1CB8 4>AO3=CB> 70 4>?><>3>N  
?>ABV9=>W 2=CB@VH=L>25==>W V=DC7VW, O:C ?>G8=0NBL I5 4> <><5=BC 22545==O  
:>=B@0AB=>3> ?@5?0@0BC V ?@>4>26CNBL 4> <><5=BC 9>3> 282545==O =8@:0<8;  
70?>1V30==O 4>40B:>2>3> =020=B065==O =0 =8@:8, I> 28=8:0T ?@8 70AB>AC20==V  
=5D@>B>:A8G=8E ?@5?0@0BV2, 70A>1V2 4;O ?5@>@0;L=>W E>;5F8AB>3@0DVW, ?@8  
?5@5B8A:0==V =8@:>28E 0@B5@V9, 0=3V>?;0AB8:8 =8@:>28E 0@B5@V9, EV@C@3VG=8E  
>?5@0FVOE, 4> 282545==O :>=B@0AB=>W @5G>28=8 7 >@30=V7  
?>2B>@=V @5=B35=>:>=B@0AB=V 4>A;V465==O ?>B@V1=> ?@>2>48B8 ?VA;O ?>2=>W =>@  
<0;V70FVW DC=:FV9 =8@>: ?VA;O >AB0==L>3> 22545==O ?@5?0@0BC.  
0FVT=B8 7 FC:@>28< 4V015B><, O:V 70AB>A>2CNBL B5@0?VN <5BD>@0AB>AC20==O 9>4>2  
=B@0AB=8E @5G>28= E2>@8< =0 FC:@>289 4V015B, O:V ?@89<0NBL <5BD>@A>1;82> ?0FVT=B0< 7  
?>@CH5==O< DC=:FV9 =8@>:, <>65 ?@872>48B8 4> ;0:B>0F84>7C.  
;O ?>?5@5465==O ;0:B>F84>7C C ?0FVT=BV2 7 FC:@>28< 4V015B><, O:V 70AB>A>2CNBL B5@0?VN  
<5BD>@<, ?5@54 2=CB@VH=L>AC48==8< 22545==O< :>=B@0AB=>3> 70A>1C, I> 24, =5>1EV4=> 28  
20B:8 :@>2V B0 268B8 70?>1V6=8E 70E>4V2 C =86G5707=0G5=8E 28?04:0E.  
>@<0;L=89 @V25=L :@50B8=V=C A8@>20B:8 :@>2V (<130. @89>< <5BD>@ A;V4 ?@8?8=8B8 ?V4  
G0A 22545==O :>=B@0AB=>3> 70A>1C V =5 2V4=>2;N20B8 ?@>BO3><  
48 3>48= 01> 4> 2V4=>2;5==O DC=:FV9 =8@>:/:@50B8=V=C A8@>20B:8 :@>2V 4> =>@<0;L=>3>  
@V2=O.  
V428I5==O @V2=O :@50B8=V=C A8@>20B:8 :@>2V (>130. !;V4 ?@8?8=8B8 ?@89>< <5BD>@  
1AB565==O :>=B@0AB=8< 70A>1>< =0 48 3>48=. "5@0?VN <5BD>@< ?>=>2;NNBL BV;L:8 C @07V,  
O:I> DC=:FVW =8@>:/:@50B8=V=C A8@>20B:8 :@>2V 70;8H0NBLAO =57@CH5==O DC=:FV9 =8@>:  
01> AB0= WE =52V4><89, ;V:0@ ?>28=5= >FV=8B8 A?V22V4=>H5==O @878:/:>@8ABL 4;O ?0FVT=B0  
2V4 70AB>AC20==O ?@5?0@0BC V 268B8 70?>1V6=8E 70E>4V2: ?@8?8=8B8 ?@89>< <5BD>@1;82>  
206;828< T 70157?5G5==O 045:20B=>W 3V4@0B0FVW ?0FVT=BV2 ?5@54 B0 ?@>BO3>< 24 3>48=  
?VA;O 22545==O :>=B@0AB=>3> 70A>1C. !;V4 :>=B@>;N20B8 DC=:FVN =8@>: (7>:@5<0, :@50B8=V=  
A8@>20B:8), @V25=L <>;>G=>W :8A;>B8 C A8@>20BFV :@>2V B0pH :@>2V.  
A=CT ?>B5=FV9=89 @878: @>728B:C ?5GV=:>2>W =54>AB0B=>ABV.A>1;82> >15@56=8<8 A;V4 1CB8  
7 E2>@8<8 7 BO6:8<8 :><1V=>20=8<8 ?>@CH5==O<8 DC=:FV9 =8@>: V ?5GV=:8, >A:V;L:8 C 40=>W  
3@C?8 ?0FVT=BV2 A?>AB5@V30TBLAO 7=0G=5 7=865==O ;V@5=AC :>=B@0AB=8E @5G>28=  
0FVT=B8 =0 35<>4V0;V7V <>6CBL >B@8=B@0AB=C @5G>28=C 4;O @04V>;>3VG=8E ?@>F54C@.  
5<0T =5>1EV4=>ABV :>@5;OFVW G0AC  
0AB>AC20==O 9>4>2:>=B@0AB=8E @5G>28= <>65 ?>A8;N20B8 A8<8 =0==V V=20782=8E 2B@CG0=L  
E2>@8< =0 D5>E@><>F8B>1EV4=5 ?@>DV;0:B8G=5 70AB>AC20==O 0;LD0-1;:>0B>@V2 4;O  
70?>1V30==O @>728B:C 3V?5@B>=VG=8E :@87V2. 5>1EV4=0 >A>1;820 >15@56=VABL ?@8  
>1AB565==V ?0FVT=BV2 7 3V?5@B8@5>W487<>@8E 7 1030B>2C7;>28< 7>1>< ?VA;O 22545==O 9>4>2  
=B@0AB=8E 70A>1V2 VA=CT @878: @>728B:C 3V?5@B8@5>W487  
8EV4 :>=B@0AB=>3> 70A>1C V7 AC48= @V4:> AC?@>2>46C202AO  
03;04 70 ?0FVT=B> VA;O 22545==O :>=B@0AB=>3> ?@5?0@0BC A;V4 A?>AB5@V30B8 70 AB0=<  
?0FVT=B0 ?@>BO3>< O:

=B@0B5:0;L=5 22545==O. VA;O 28:>=0==O3@0DVW ?0FVT=B ?>28=5= ?5@51C20B8 C A?>:>W =5  
<5=H5 1 3>48=8, ;560G8 7 ?V4=OB>N =0 20° 3>;>2>N B0 3@C4=>N ;;VB:>N. VA;O FL>3> E2>@>3>  
<>6=0 ?5@52>48B8 =0 0<1C;0B>@=89 @568<, >4=0: ?0FVT=B ?>28=5= C=8:0B8 =0E8;V2. @8 4>B@8  
<0==V ?>ABV;L=>3> @568 ?V4=OB5 ?>;>65==O 3>;>28 B0 3@C459 ?>28==> 715@V30B8AO  
?@>BO3<< ?5@H8E

6 3>48=. @8 ?V4>7@V =0 =87L:89 ?>@V3 @>728B:C AC4< =5>1EV4=> A?>AB5@V30B8 70  
4>A;V46C20=8< ?@>BO3<< FL>3> ?5@V>4C. <1C;0B>@=V ?0FVT=B8 ?@>BO3<< ?5@H8E 24 3>48=  
?VA;O 4>A;V465==O =5 ?>28==V 70;8H0B8AO =0 A0<>BV.

A>1;82>ABV 70AB>AC20==O 4VBO!;V4 ?0<□OB0B8 ?@> <>6;82VABL @>728B:C B@0=78B>@=>3>  
3V?>B8@5>W487=>H5=8E, =>2>=0@>465=8E B0 V=H8E 4VB59 C 72O7:C 7 22545==O< 9>4>2  
:=>B@0AB=8E @5G>28=. 54=>=>H5=V 4VB8 <0NBL ?V428I5=C GCB;82VABL 4> 9>4C. 5>1EV4=>  
:=>B@>;N20B8 DC=:FVN I8B>284=>W 70;>78. @8 70AB>AC20==V 9>4>2=B@0AB=8E @5G>28=  
203VB=8< 6V=:0< A;V4 :=>B@>;N20B8 DC=:FVN I8B>284=>W 70;>78 C =>2>=0@>465=8E ?@>BO3<<  
?5@H>3> B86=O 68BBO.

A>1;82> =5<>2;OB0< 4> B0 ?VA;O 22545==O :=>B@0AB=>3> ?@5?0@0BC =5>1EV4=> 70157?5G8B8  
045:20B=C 3V4@0B0FVN. V:C20==O =5D@>B>:A8G=>ABV <0T 1CB8 72065=8 2V4 2V:C 7  
<5=HCTBLAO H284:VABL ;;C1>G:>2>W DV;LB@0FVW C =5>2;OB, I> <>65 ?@8725AB8 4> 70B@8  
=B@0AB=8E @5G>28=.

# 4VB59 2V:<< 4> >4=>3> @>:C B0 >A>1;82> C =>2>=0@>465=8E ?>@CH5==O 35<>48=0;VB=>3>  
10;0=AC 2V41C20TBLAO >A>1;82> ;53:>.  
&59 ;V:0@AL:89 70AV1

**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.**

>4=8E 4>A;V465=L 2?;82C ?@5?0@0BC =0 740B=VABL :5@C20B8 02B>B@0=A?>@B< V ?@0FN20B8 7  
<5E0=V7<0<8 =5 ?@>2>48;>AO. 5 @5:><5=4CTBLAO :5@C20B8 02B>B@0=A?>@B< B0 ?@0FN20B8  
7V A:;04=>N B5E=V:>N ?@>BO3<< ?5@H8E 24 3>48= ?VA;O V=B@0B5:0;L=>3> 22545==O  
:=>B@0AB=8E 70A>1V2. @8 =0O2=>ABV A82545==O 3@0DVW @VH5==O ?>B@V1=> ?@89<0B8  
V=482V4C0;L=>.

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

0AB>AC20==O 9>4>2=B@0AB=8E @5G>28= E2>@8< =0 FC:@>289 4V015B, I> ?@89<0NBL <5BD>@  
(482. @>74V; «A>1;82>ABV 70AB>AC20==O»).

0FVT=B8, I> ?@89<0;8 <5=H5 =V6 70 2 B86=V 4> 4>A;V465==O V=B5@;59:V=-2, <0NBL AE8;L=VABL  
4> 2V440;5=8E ?>1VG=8E @50:FV9 (3@8?>?>4V1=V AB0=8 01> H:V@=V @50:FVW).  
AV 9>4>2=B@0AB=V @5G>28=8 <>6CBL 270T<>4VOB8 7 4V03=>AB8G=8<8 B5AB0<8 4>A;V465=L  
DC=:FV9 I8B>284=>W 70;>78, B>284=>W 70;>78 72O7C20B8 9>4 <>65 7=86C20B8AL =0 ?5@V>4 4>  
45;V;L:>E B86=V2.

8A>:0 :=>F5=B@0FVO :=>B@0AB=8E 70A>1V2 C A8@>20BFV :@>2V V A5GV<>65 2?;820B8 =0  
@57C;LB0B8 ;01>@0B>@=8E ?>:07=8:V2 1V;V@C1V=C, 1V;;V2 V =5>@30=VG=8E A?>;C: (=0?@8:;04,  
70;V70, AD0BV2), B>@0B>@=V 0=0;V78 =5 A;V4 ?@>2>48B8 C B>9 65 45=L.

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

\$0@<0:>48=0

>35:A>; =5V>==89, <>=><5@=89, B@89>4>20=89, 2>4>@>7G8==89 @5=B35=>:=>B@0AB=89 70AV1.  
@8 4>A;V465==V 74>@>28E 4>1@>2>;LFV2 ?VA;O 2=CB@VH=L>25==>W V=T:FVW 9>35:A>;C =5  
1C;> 2AB0=>2;5=> 7=0GCI8E 2V4E8;5=L 1V;LH>ABV ?>:07=8:V2 35<>48=0-1V>EV:07=8:V2 B0  
?>:07=8:V2 :=>03C;OFVW. @0B>@=8E ?>:07=8:V2 1C;8 =57=0G=8<8 V =5 22060NBLAO ;;V=VG=>  
7=0GCI8<8.

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

@81;87=> 100 % 22545=>3> 2=CB@VH=L>25==> 9>35:A>;C 2840;OTBLAO C =57@<0;L=>  
DC=:FV>=CNGV =8@:8 ?@>BO3<< 24 3>48=. 5@V>4 =0?V2282545==O ?@5?0@0BC C ?0FVT=V2 V7  
=>@<0;L=>N DC=:FVTN =8@>: AB0=>28BL 2 3>48=8. 5B01>;VBV2 ?@5?0@0BC =5 2AB0=>2;5=>.  
2O7C20==O 9>35:A>;C 7 1V;;0<8 ?;07<8 =5 <0T ;;V=VG=>3> 7=0G5==O (<5=H5 2 %) V B> C2038 <>65  
=5 1@0B8AO.



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

A=>2=V DV78:>-EVABV: ?@>7>@0 15710@2=0 01> A2VB;>-6>2B>3> :>;L>@C @V48=0 (@>7G8=).

"5@ABV. 3 @>: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 2 >@83V=0;L=V9 C?0:>2FV 2 70E8I5=>@8==>3> @5=B35=V2AL:>3> 28?@>

#?0:>2:0.

> 20 <; 2 0 5 0

> 20 <; 01> 50 <;, 01> 100 <; C D;0:>=V. > 1 D;0:>=C C ?0GFV.

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

8@>1=8:.

" «\$0@<0:».

VAF57=0E>465==O.

#:@0W=0, 04080, <. 8W2, 2C;. \$@C=75, 63.

!" #&/  
>? <548F8=A:>

"□ !□  
(TOMOHEXOL)

!>AB02:

459AB2CNI55 25I5AB2>: iohexol;

1 <; @0AB2>@0 A>45@68B 9>35:A>;0 2 ?5@5AG5B5 =0 100 % 25I5AB2>, GB> M:2820;5=B=> 9>4C:

<3 9>40/<;	240	300	350
<3 9>35:A>;0/<;	518	647	755

2A?><>30B5;L=K5 25I5AB20: =0B@8O :0;LF8O M45B0B, B@><5B0<8=, :8A;>B0

E;>@8AB>2>4>@>4=0O @072545==0O, 2>40 4;O 8=J5:F89.

5:0@AB25==0O D>@<0. 0AB2>@ 4;O 8=J5:F89.

\$0@<0:>B5@0?52B8G5A:0O 3@C??0. >4A>45@60I85 @5=B35=>:>=B@0AB=K5 A@54AB20.

>4>@0AB2>@8>A<>;O@=K5 =5D@>B@>?=K5 @5=B35=>:>=B@0AB=K5 A@54AB20.

>4 " ! V08A B02.

;8=8G5A:85 E0@0:B5@8AB8:8.

>:070=8O.

"><>35:A>; ?@54=07=0G5= B>;L:> 4;O 4803=>AB8G5A:8E F5;59.

5=B35=>:>=B@0AB=K9 ?@5?0@0B 4;O ?@8<5=5=8O 45BO< 8 27@>A;K< A F5;LN ?@>2545=8O

:0@48>0=38>3@0D88, 0@B5@8>3@0D88, C@>3@0D88, D;51>3@0D88 8 :>=B@0AB=>3> CA8;5=8O

?@8 :>9 B><>3@0D88 (" ); ?@8 ?>OA=8G=>9, 3@C4=>9 8 H59=>9 <85;>3@0D88, "-F8AB5@=>3@0D88

?>A;5 AC10@0E=>840;L=>3> 22545=8O; 0@B@>3@0D88, M=4>A:>?8G5A:>9 @5B@>3@04=>9

?0=:@50B>3@0D88 (- ), M=4>A:>?8G5A:>9 @5B@>3@04=>9 E>;0=38>?0=:@50B>3@0D88 (- %),

35@=8>3@0D88, 38AB5@>A0;L?8=3>3@0D88, A80;>3@0D88 8 8AA;54>20=8OE 65;C4>G=>-.8H5G=>3>

B@0:B0.

@>B82?>:070=80.

>2KH5==00 GC2AB28B5;L=>ABL : 9>4C 8;8 : 4@C38< :>=5=B0< ?@5?0@0B0. K@065==K9  
B8@5>B>:A8:>7. -?8;5?A8O 8 F5@51@0;L=K5 8=D5:F88 (4;O AC10@0E=>840;L=>3> 22545=80).

!?!>A>I ?@8<5=5=80 8 4>7K.

;O 2=CB@80@B5@80;L=>3>, 2=CB@825==>3>, 8=B@0B5;0;L=>3>, 2=CB@8?>;>AB=>3> 22545=80,  
?5@>@0;L=>3> ?@85<0 8 @5:B0;L=>3> 22545=80 27@>A;K< 8 45BO  
>70 ?@5?0@0B0 7028A8B >B <5B>40 8AA;54>20=80, 2>7@0AB0, <0AAK B5;0, <8=CB=>3> >1J5<0  
A5@4F0, >1I53> A>AB>O=80 ?0F85=B0 8 B5E=8:8 ?@8<5=5=80 ?@5?0@0B0. 5@54 8 ?>A;5 ?@8  
<5=5=80 :>=B@0AB=>3> 25I5AB20, B0: :0: 8 4;O 4@C38E @5=B35=>:>=B@0AB=KE A@54AB2,  
=5>1E>48<> >15A?5G8BL A>>B25BAB2CNICN 384@0B0F8N >@30=87<0.

>:070=80	>=F5=B@0F80 9>40, <3/<;	1J5< ?@5?0@0B0, <;	A>1K5 C:070=80
=CB@825==>5 22545=85			
#>3@0D80			
7@>A;K5	300 8;8 350	40-80	>B45;L=KE A;CG0OE 2>7<>6=> 22545=85 1>;55 80 <;
5B8 (<0AA0 B5;0 <5=55 7 :3)	240 300	4 <;/:3 3 <;/:3	
5B8 (<0AA0 B5;0 1>;55 7 :3)	240 300	3 <;/:3 2 <;/:3	
\$;51>3@0D80 (=86=85 :>=5G=>AB8)	240 8;8 300	20-100 (=0 >4=C :>=5G=>ABL)	<0:A. 4>70 40 <;
&8D@>200 AC1B@0:F8>==00 0=38>3@0D80	300 8;8 350	20-60	
#A8;5=85 ?@8 "			
7@>A;K5	240	100-250	1I55 :>;8G5AB2> 9>40 2 8=J5:F88 >1KG=> A>AB02;O5B 30-60 3
	300	100-200	
	350	100-150	
5B8	240	2-3 <;/:3 (4> 40 <;)	>B45;L=KE A;CG0OE 2>7 <>6=> 22545=85 4> 100 <;
	300	1-3 <;/:3 (4> 40 <;)	
=CB@80@B5@80;L=>5 22545=85			
@B5@8>3@0D80:			
4C30 0>@BK	300	30-40	1J5< =0 >4=C 8=J5:F8N 7028A8B >B <5AB0 22545=80
A5;5:B82=00 F5@51@0;L=00 0=38>3@0D80	300	5-10	
0>@B>3@0D80	350	40-60	
0=38>3@0D80 154@5==KE 0@B5@89	300 8;8 350	30-50	
?@>G85 284K	300	7028A8B >B <5B>40 8AA;54>20=80	
0@48>0=38>3@0D80:			
7@>A;K5 ;52K9 65;C4>G5; :>@5=L 0>@BK, A5;5:B82=00 :>@>=0@>3@0D80	350  350	30-60  4-8	

5B8	300 8;8 350	>70 7028A8B >B 2>7@0AB0, <0AAK B5;0 8 701>;520=8O	<0:A. 4>70 8 <;/:3
<b>&amp;8D@&gt;200 AC1B@0:F8&gt;==0O 0=38&gt;3@0D8O</b>	240 8;8 300	1-15	7028A8<>AB8 >B <5AB0 22545=8O <>3CB 1KBL 8A?>;L7>20=K >1JQ 30 <;
<b>=B@0B5:0;L=&gt;5 22545=85</b>			
<b>&gt;OA=8G=0O 8 3@C4=0O &lt;85;&gt;3@0D8O</b>	240	10-15 8-12	;N<10;L=>5 22545=85
<b>(59=0O &lt;85;&gt;3@0D8O</b>	240	10-12	;N<10;L=>5 22545=85
	300	7-10	22545=85
	240	6-10	1>:>2>5 H59=>5 22545=85
	300	6-8	
<b>" F8AB5@=&gt;3@0D8O</b>	240	4-12	;N<10;L=>5 22545=85
<b>=CB@8?&gt;;&gt;AB=&gt;5 22545=85</b>			
<b>@B@&gt;3@0D8O</b>	240	5-20	
	300	5-15	
	350	5-10	
<b>- /- %</b>	240	20-50	
<b>5@=8&gt;3@0D8O</b>	240	50	1J5< 22545=8O 7028A8B >B >1JQ<0 3@K68
<b>8AB5@&gt;A0;L?8=3&gt;3@0D8O</b>	240	15-50	
	300	15-25	
<b>!80;&gt;3@0D8O</b>	240 8;8 300	0,5-2	
<b>5@&gt;@0;L=&gt;5 ?@8&lt;5=5=85</b>			
<b>AA;54&gt;20=85 "</b>			
<b>7@&gt;A;K5</b>	350	?@545;O5BAO 8=48284C0;L=>	
<b>5B8 (?8I52&gt;4)</b>	300 8;8 350	2-4 <;/:3	0:A8<0;L=0O 4>70 50 <;
<b>54&gt;=&gt;H5==K5 45B8</b>	350	2-4 <;/:3	
<b>#A8;5=85 ?@8 "</b>			
<b>7@&gt;A;K5</b>	0725AB8 2>4>9 4> :=F5=B@0F88 >:>;> 6 <3 9>40/ <;	800-2000 <; ?>;CG5==>3> @0AB2>@0 2 B5G5=85 >?@545;5==>3> ?5@8>40	0?@8<5@: @0725AB8 "> <>35:A>;-300 8;8 "> <>35:A>;-350 2>4>9 1:50.
<b>5B8</b>		15-20 <; ?>;CG5==>3> @0AB2>@0/:3 <0AAK B5;0	
<b>5:B0;L=&gt;5 22545=85</b>			
<b>#A8;5=85 ?@8 "</b> 5B8	0725AB8 2>4>9 4> :=F5=B@0F88 >:>;> 6 <3 9>40/ <;	K18@05BAO 8=48284C0;L=>	0?@8<5@: @0725AB8 "> <>35:A>;-300 8;8 "> <>35:A>;-350 2>4>9 1:50.

AA;54>20=85 " 5B8	240 8;8 300, 8;8 350 @0725AB8 2>4>9 4> :=F5=B@0F88 100-150 <3 9>40/<;	5-10 <;/:3 ?>;CG5==>3> @0AB2>@0	0?@8<5@: @0725AB8 "<> 35:A>;-240, "<>35:A>;-300 8;8 "<>35:A>;-350 2>4>9 1:1 8;8 1:2
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>I>G=K5 @50:F88.

1I85 284K ?>1>G=KE @50:F89 (E0@0:B5@=K5 4;O 2A5E 9>4A>45@60I8E @5=B35=>:=B@0AB=KE A@54AB2).

865 ?@82545=K 2>7<>6=K5 >A=>2=K5 ?>1>G=K5 5DD5:BK, A2O70==K5 A ?@>2545=8< @5=B35=>;>38G5A:8E ?@>F54C@ A ?@8<5=5=85< =58>==KE :=B@0AB=KE A@54AB2.  
50:F88 38?5@GC2AB28B5;L=>AB8 <>3CB 2>7=8:0BL =57028A8<> >B 4>7K 22>48<>3> ?@5?0@0B0 8 A?>A>10 22545=8O. 53:85 A8

"@0=78B>@=>5 ?>2KH5=85 S-:@50B8=8=0 G0AB>5 O2;5=85 ?>A;5 ?@8<5=5=8O 9>4A>45@60I8E @5=B35=>:=B@0AB=KE A@54AB2, ?>2KH05BAO @8A: 2>7=8:=>25=8O :=B@0AB8=4CF8@>20==>9 =5D@>?0B88.

>487< 8;8 9>4=K9 ?0@>B8B >G5=L @54:0O @50:F8O =0 22545=85 9>4A>45@60I8E @5=B35=>:=B@0AB=KE A@54AB2. =0 <>65B 2K@060BLAO 2 2845 >B5:0 8 1>;8 2 A;N==KE 65;570E 2 B5G5=85 10 4=59 ?>A;5 8AA;54>20=8O.

!> AB>@>=K 8<9 A8AB5@50:F88 38?5@GC2AB28B5;L=>AB8 (2;;NG0O >4KH:C, AK?L, M@8B56=K5 @50:F88, 20A:C;8B, 0=38=>52@>B8G5A:89 >B5.; >B5: 3>@B0=8, ;0@8=3>A?07<, 1@>=E>A?07< 8;8 =5:0@48>35==K9 >B5: ;53:8E <>3CB @072820BLAO :0: =5?>A@54AB25==> ?>A;5 22545=8O ?@5?0@0B0, B0: 8 G5@57 =5A>;L:> 4=59), 0=0D8;0:B8G5A:85/0=0D8;0:B>84=K5 @50:F88, 0=0D8;0:B8G5A:89/0=0D8;0:B>84=K9 H>..

!> AB>@>=K =5@2=>9 A8AB53>;>2=0O 1>;L, 48A35278O (?@5E>4OI89 <5B0;;8G5A:89 ?@82:CA), 207>2030;L=0O ?>B5@O A>7=0=8O.

!> AB>@>=K A5@45G=>-A>AC48AB>9 A8AB5 1@048:0@48O, 0@B5@80;L=0O 38?5@B5=78O, 0@B5@80;L=0O 38?>B5=78O.

!> AB>@>=K ?8I520@8B5;L=>9 A8AB5 B>H=>B0, @2>B0, 480@5O, 1>;L/48A:>@B 2 M?830AB@0;L=>9 >1;0AB8, C25;8G5=85 @07<5@>2 A;N==KE 65;57.

1I85 @0AAB@>9AB20: >IC15=85 60@0, ?8@5:A8O, 4@>60=85 (>7=>1).

"@02B@02;5=8O 8 >A;>6=5=8O ?@>F54C@: 9>487

>1>G=K5 @50:F88, A2O70==K5 A 2=CB@8A>AC48ABK< (2=CB@80@B5@80;L=K< 8 2=CB@825==K<) 22545=85

0728B85 ?>1>G=KE @50:F89, :=B>@K5 <>3CB =01;N40BLAO 2> 2@53> 22545=8O, 7028A8B >B <5AB0 8=J5:F88 8 4>7K ?@5?0@0B0. @8 A5;5:B82=>9 0=38>3@0D88 8 4@C38E 8AA;54>20=8OE, :=340 :=B@0AB=>5 A@54AB2> 2 2KA>;>9 :=F5=B@0F88 ?@>=8:05B 2 8AA;54C5@30=, <>3CB =01;N40BLAO =0@CH5=8O DC=:F89 40==>3> >@30=0.

!> AB>@>=K 8<9 A8AB5@50:F88 38?5@GC2AB28B5;L=>AB8, 2;;NG0O >?0A=CN 4;O 687=8 8;8 ;5B0;L=CN 0=0D8;0:A8N, BO65;K5 ?CABC;57=K5, M:AD>;80B82=K5 8;8 1C;;57=K5 @50:F88.

!> AB>@>=K M=4>:@8==>9 A8AB5B8@5>B>:A8:>7, B@0=78B>@=K9 38?>B8@5>8487

!> AB>@>=K ?A8E8:8: A?CB0==>ABL A>7=0=8O.

!> AB>@>=K =5@2=>9 A8AB53>;>2>:@C65=85, AC4>@>38, =0@CH5=85 A>7=0=8O, M=F5D0;>?0B8O, ABC?>@, @0AAB@>9AB20 GC2AB28B5;L=>AB8 (2;;NG0O 38?5AB578N), ?0@5AB578O, B@5<>@, 3>;>2=0O 1>;L, 48A35278O, B@0=78B>@=0O <>B>@=0O 48ADC=:F8O (2;;NG0O @5G52K5 @0AAB@>9AB20, 0D078N, 4870@B@8N), B@0=78B>@=0O :=B@0AB=0O M=F5D0;>?0B8O (2;;NG0O B@0=78B>@=CN 35<8?;538N 8;8 45;8@89, 2@5<5==CN ?>B5@N ?0@85=B0F8N, :=3@04=CN 0<=578N).

!> AB>@>=K >@30=>2 7@5=8O: B@0=78B>@=0O :=@:>20O A;5?>B0.

!> AB>@>=K >@30=>2 A;CE0 8 @02=>25A8O: B@0=78B>@=0O ?>B5@O A;CE0.

!> AB>@>=K A5@45G=>-A>AC48AB>9 A8AB50@8B<8O (2;;NG0O 1@048:0@48N, B0E8:0@48N), 8=D0@:B <8>:0@40, 38?5@5<8O, 0@B5@80;L=0O 38?5@B5=78O, BO65;K5 >A;>6=5=8O A> AB>@>=K A5@4F0 (2;;NG0O >AB0=>2:C A5@4F0, :0@48>@5A?8@0B>@=CN >AB0=>2:C), A?07< :=@>=0@=KE 0@B5@89, 1>;L 2 3@C48, H>.:, 0@B5@80;L=K9 A?07<, 8H5<8O, B@><1>D;518B 8 B@><1>7.

!> AB>@>=K 4KE0B5;L=>9 A8AB5:0H5;L, 48A?=>M, =5:0@48>35==K9 >B5: ;53:8E, >AB@K5  
@5A?8@0B>@=K5 A8=E>A?07<, ;0@8=3>A?07<, ?@8ABC? 0AB  
!> AB>@>=K ?8I520@8B5;L=>9 A8AB5480@5O, B>H=>B0, @2>B0, C25;8G5=85 A;N==KE 65;57, 1>;L 2  
682>B5, >1>AB@5=85 ?0=@50B8B0, >AB@K9 ?0=@50B8B.  
!> AB>@>=K :>68 8 ?>4:>6=KE B:0=59: @<=0O M@8B5<0, >AB@K9 35=5@0;87>20==K9 M:70=B5  
<0B>7=K9 ?CABC;57, 1C;;57=K9 45@<0B8B, A8=4@< !B825=A0-6>=A>=0, B>:A8G5A:89 M?845@  
<0;L=K9 =5:@>;87, <548:0<5=B>7=0O :>6=0O @50:F8O, A?>@>2>640NI0OAO M>78=>D8;859 8 A8AB5  
<=K<8 ?@>O2;5=8O<8, 2=570?=>5 >1>AB@5=85 ?A>@8070.  
!> AB>@>=K >?>@=>-42830B5;L=>3> 0??0@0B0 8 A>548=8B5;L=>9 B:0=8: 0@B@0;38O.  
!> AB>@>=K ?>G5: 8 <>G52K2>4O18E ?CB59: =0@CH5=85 DC=:F89 ?>G5.; 2;;NG0O >AB@CN  
?>G5G=CN =54>AB0B>G=>ABL.  
I185 @0AAB@>9AB20 8 87<5=5=8O 2 <5AB5 22545=8O: >ICI5=85 60@0, 1>;L 8 48A:>@B,  
0AB5=8G5A:>5 A>AB>O=85 (2;;NG0O =54<>30=85, CB<;5=85), 4@>60=85 (>7=>1), 38?5@B5@<8O,  
@50:F88 2 <5AB5 22545=8O, 2;;NG0O B@0=AAC40F8N, 1>;L 2 A?8=5.  
=B@0B5:0;L=>5 22545=85.  
>1>G=K5 @50:F88 <>3CB 2>7=8:0BL G5@57 =5A:>;L:> G0A>2 8;8 4=59 ?>A;5 8=B@0B5:0;L=>3>  
22545=8O. E G0AB>B0 ?@81;878B5;L=> >B25G05B G0AB>B5 >A;>6=5=89 ?>A;5 ;N<10;L=KE ?C=:F89  
157 22545=8O :=B@0AB=>3> A@54AB20. ;O B>3>, GB>1K <8=8<878@>20BL A=865=85 402;5=8O,  
A;54C5B ?@54>B2@0I0BL G@57<5@=>5 2K2545=85 A?8==><73>2>9 684:>AB8.  
!> AB>@>=K 89 A8AB5@50:F88 38?5@GC2AB28B5;L=>AB8, 2;;NG0O 0=0D8;0:B8G5A:85  
/0=0D8;0:B>84=K5 @50:F88.  
!> AB>@>=K ?A8E8:8: A?CB0==>ABL A>7=0=8O.  
!> AB>@>=K =5@2=>9 A8AB53>;>2=0O 1>;L (<>65B 1KBL A8;L=>9 8 4;8B5;L=>9), 0A5?B8G5A:89  
<5=8=38B (2;;NG0O E8<8G5A:89 <5=8=38B), AC4>@>38, 3>;>2>:@C65=85, 48A35278O, 207>2030;L=>5  
A8=:>?5, =0@CH5=85 @8B<0 M=F5D0;>3@0< B@0=78B>@=CN 35<8?;538N 8;8 45;8@89, 2@5<5==CN  
?>B5@N ?0@, @5B@>3@04=CN 0<=578N), B@0=78B>@=0O <>B>@=0O 48ADC=:F8O (2;;NG0O  
@5G52K5 @0AAB@>9AB20, 0D078N, 4870@B@8N), ?0@5AB578O, 38?5AB578O, @0AAB@>9AB20  
GC2AB28B5;L=>AB8.  
!> AB>@>=K >@30=>2 7@5=8O: B@0=78B>@=0O :=@>20O A;5?>B0, A25B>1>O7=L.  
!> AB>@>=K >@30=>2 A;CE0 8 @02=>25A8O: B@0=78B>@=0O ?>B5@O A;CE0.  
!> AB>@>=K ?8I520@8B5;L=>9 A8AB51>;L 2 682>B5, C25;8G5=85 A;N==KE 65;57, B>H=>B0, @2>B0,  
480@5O.  
!> AB>@>=K >?>@=>-42830B5;L=>3> 0??0@0B0 8 A>548=8B5;L=>9 B:0=8: 1>;L 2 H55, 1>;L 2  
A?8=5, A?07  
I185 @0AAB@>9AB20 8 87<5=5=8O 2 <5AB5 22545=8O: 1>;L 2 :=5G=>ABOE, >ICI5=85 60@0,  
?8@5:A8O, 4@>60=85 (>7=>1), 87<5=5=8O 2 <5AB5 22545=8O.  
>1>G=K5 @50:F88, A2O70==K5 A 2=CB@8?>;>AB=K< 22545=85  
!> AB>@>=K 8<9 A8AB5@50:F88 38?5@GC2AB28B5;L=>AB8, 2;;NG0O 0=0D8;0:B8G5A:85  
/0=0D8;0:B>84=K5 @50:F88.  
!> AB>@>=K =5@2=>9 A8AB53>;>2=0O 1>;L, 48A35278O, 207>2030;L=>5 A8=:>?5.  
!> AB>@>=K ?8I520@8B5;L=>9 A8AB5B>H=>B0, 1>;L 2 682>B5, C25;8G5=85 A;N==KE 65;57, @2>B0,  
480@5O; ?@8 38AB5@>A0;L?8=3>3@0D88 1>;L 2=87C 682>B0.  
I185 @0AAB@>9AB20 8 87<5=5=8O 2 <5AB5 22545=8O: >ICI5=85 60@0, ?8@5:A8O, 4@>60=85 (>7=>1).  
5@>@0;L=>5 ?@8<5=5=85.  
!> AB>@>=K ?8I520@8B5;L=>9 A8AB5480@5O, B>H=>B0, @2>B0, 1>;L 2 682>B5.  
8AB5@>A0;L?8=3>3@0D8O (!).  
!> AB>@>=K ?8I520@8B5;L=>9 A8AB51>;L 2 =86=8E >B45;0E 682>B0.  
@B@>3@0D8O.  
!> AB>@>=K >?>@=>-42830B5;L=>3> 0??0@0B0 8 A>548=8B5;L=>9 B:0=8: 0@B@8B.  
I185 @0AAB@>9AB20 8 =0@CH5=8O 2 <5AB5 22545=8O: 1>;L.  
B45;L=K5 ?>1>G=K5 @50:F88.  
!>>110;>AL > @0728B88 B@><1>M<1>;8G5A:8E >A;>6=5=89 2 A2O78 A ?@>2545=85< :=B@0AB=>9  
0=38>3@0D88 :=@>=0@=KE, <>73>2KE, ?>G5G=KE 8 ?5@8D5@8G5A:8E 0@B5@89. :=B@0AB=>5  
25I5AB2> <>65B A?>A>1AB2>20BL @0728B8N >A;>6=5=89 (A<. @0745; «A>15==>AB8 ?@8<5=5=8O»)).  
!>>110;>AL > @0728B88 >A;>6=5=89 A> AB>@>=K A5@4F0, 2;;NG0O >AB@K9 8=D0@:B<8>:0@40 2>

2@5A;5 ?@>2545=8O :=B@0AB=>9 :>@>=0@=>9 0=38>3@0D88. 0F85=BK ?>68;>3> 2>7@0AB0 8;8  
?0F85=BK A BO65;>9 8H5<8G5A:>9 1>;57=LN A5@4F0, =5AB018;L=>9 AB5=>:0@4859 8 48ADC=:F859  
;52>3> 65;C4>G:0 8<5;8 1>;55 2KA>:89 @8A: @0728B8O >A;>6=5=89 (A15==>AB8 ?@8<5=5=8O»).

548=8G=KE A;CG0OE :=B@0AB=>5 A@54AB2><65B ?@>=8:0BL G5@57 35<0B>M=F5D0;8G5A:89  
10@L5@, 2 @57C;LB0B5 G53> 2>7=8:05B =0:>?;5=85 ?@5?0@0B0 2 :>@5 3>;>2=>3> <>730, GB> <>65B  
2K720BL =52@>;>38G5A:85 @50:F88, 2;;NG0O AC4>@>38, B@0=78B>@=K5 <>B>@=K5 8;8  
A5=A>@=K5 @0AAB@>9AB20, B@0=78B>@=>5 =0@CH5=85 A>7=0=8O, B@0=78B>@=CN ?>B5@N ?>  
?0B8N (A15==>AB8 ?@8<5=5=8O»).

=0D8;0:B>84=K5 @50:F88 8 0=0D8;0:B>84=K9 H>: <>65B ?@825AB8 : 3;C1>:>9 38?>B5=788 8  
A2O70==K < A =59 A8<0<, 2;;NG0O 38?>:A8G5A:CN M=F5D0;>?0B8N, ?>G5G=CN 8 ?5G5=>G=CN  
=54>AB0B>G=>ABL (A15==>AB8 ?@8<5=5=8O»).

=5:>B>@KE A;CG0OE B@0=AAC40F8O :=B@0AB=>3> 25I5AB20 2K7K205B ;>:0;L=CN 1>;L 8 >B5:,  
:>B>@K5 >1KG=> ?@>E>4OB 157 >A;>6=5=89. 0D8:A8@>20=K A;CG08 2>A?0;5=8O, =5:@>70 B:0=59 8  
:><0 (A<. @0745; «A>15==>AB8 ?@8<5=5=8O»).

0F85=BK 45BA:>3> 2>7@0AB0. !;54C5B ?><=8BL > 2>7<>6=>AB8 @0728B8O B@0=78B>@=>3>  
38?>B8@5>8487<0 C =54>=>H5==KE, =>2>@>645==KE 8 4@C38E 45B59 2 A2O78 A 22545=85<  
9>4A>45@60I8E :=B@0AB=KE 25I5AB2.

54>=>H5==K5 45B8 8<5NB ?>2KH5==CN GC2AB28B5;L=>ABL : 9>4C. !>>1I0;>AL > @0728B88  
B@0=78B>@=>3> 38?>B8@5>8487<0 C =54>=>H5==KE 45B59, =0E>4OI8EAO =0 3@C4=>> 2A:0@  
<;820=88. >35:A>; =5>4=>:@0B=> =07=0G0;8 65=I8=0<, :>@3@C4LN (A15==>AB8 ?@8<5=5=8O»).

A>15==> <;045=F0< 4> 8 ?>A;5 22545=8O :=B@0AB=>3> ?@5?0@0B0 =5>1E>48<> >15A?5G8BL  
045:20B=CN 384@0B0F8N. 5G5=85 =5D@>B>:A8G=>AB8 4>;6=> 1KBL 2725H5==K  
7028A8<>AB8 >B 2>7@0AB0 C<5=LH05BAO A:>@>ABL ;;C1>G:>2>9 D8;LB@0F88 C<;045=F52, GB>  
<>65B ?@825AB8 : 7045@6:5 M:A:@5F88 :=B@0AB=KE 25I5AB2.

**5@54>78@>2:0.**

>;8=8G5A:85 40==K5 A2845B5;LAB2CNB > 1>;LH>9 H8@>B5 B5@0?52B8G5A:>3> >:=0 9>35:A>;0 8  
>BACBAB288 25@E=59 3@0=8FK AB0=40@B=> 4>?CAB87 4;O 2=CB@8A>AC48AB>3> ?@8<5=5=8O.  
8A: @0728B8O A8<>2 ?5@54>78@>2:8 <8=8<0;L=K9, 5A;8 B>;L:> ?0F85=BC 2 B5G5=85 :>@>B:>3> 2@5

<5=8 =5 22>48BAO 1>;55 2000 <3/:3 9>40. ;8B5;L=>5 ?@8<5=5=85 2KA>:8E 4>7 ?@5?0@0B0 <>65B  
?>2;8OBL =0 DC=:F88 ?>G5: (?5@8>4 ?>;C2K2545=8O 2 G0A0). !;CG09=0O ?5@54>78@>2:0  
?@5?0@0B0 2>7<>6=0 ?@8 A;>6=KE 0=38>3@0D8G5A:8E ?@>F54C@0E C 45B59, >A>15==> ?@8  
CA;>288 <=>3>@07>2>3> 22545=8O 2KA>:8E 4>7.

A;CG05 ?5@54>78@>2:8 =5>1E>48<> ?@>25AB8 :>@>5:F8N =0@CH5=89 2>4=>-M;5:B@>;8B=>3>  
10;0=A0. !;54CNI85 3 4=O A;54C5B ?@>2>48BL <=>8B>@8=3 DC=:F88 ?>G5:. A;CG05 =5>1E>48<>AB8  
A;54C5B ?@8<5=8BL 35<>480;87 4;O C40;5=8O 87;8H:>2 ?@5?0@0B0. !?5F8D8G5A:>3> 0=B84>B0 =5  
ACI5AB2C5B.

**@8<5=5=85 2 ?5@8>4 15@5<5==>AB8 8;8 :>@<;5=8O 3@C4LN.**

5@5<5==>ABL. 57>?0A=>ABL ?@8<5=5=8O ?@5?0@0B0 2 ?5@8>4 15@5<5==>AB8 =5 CAB0=>2;5=0.  
57C;LB0BK M:A?5@8<5=B0;L=KE 4>;8=8G5A:8E 8AA;54>20=89, :0A0NI8EAO @5?@>4C:B82=>AB8,  
@0728B8O M<1@8>=0 8;8 ?>40, ?@>B5:0=8O 15@5<5==>AB8, ?5@8- 8 ?>AB=0B0;L=>3> @0728B8O,  
=5 C:07K20NB =0 ACI5AB2>20=85 ?@O<>3> 8;8 =5?@O<>3> 2@54=>3> 2;8O=8O. > 2>7<>6=>AB8

A;54C5B 871530BL ;CG52>3> 2;8O=8O 2 ?5@8>4 15@5<5==>AB8, =5>1E>48<> 2725H5==> ?>4>9B8 :  
=07=0G5=8N @5=B35=>2A:>3> 8AA;54>20=8O, A :=B@0AB=K < A@54AB2<< 8;8 157 =53>, 87-70 2>7  
<>6=>3> @8A:0.

"><>35:A>;® 2 ?5@8>4 15@5<5==>AB8 <>6=> ?@8<5=OBL B>;L:> 2 A;CG05 >AB@>9 =5>1E>48<>AB8  
A>3;0A=> @5:><5=40F8O< 2@0G0 8 ?>A;5 BI0B5;L=>9 >F5=:8 A>>B=>H5=8O ?>;L70/@8A:.  
>@<;5=85 3@C4LN. >=B@0AB=K5 A@54AB20 2 =57=0G8B5;L=>9 AB5?5=8 ?@>=8:0NB 2 3@C4=>5  
<>;>: > 8<8=8<0;L=>5 :>;8G5AB2> 01A>@18@C5BAO 2 :8H5G=8:5. >MB>40 <0;>25@>OB5=.

>A;5 22545=8O 9>4A>45@60I8E :=B@0AB=KE A@54AB2 65=I8=5, :>@<;5=85 3@C4LN <>6=>  
?@>4>;60BL. 8AA;54>20=88 :>;8G5AB2> 9>35:A>;0, 2K45;ONI55AO A 3@C4=K< <>;>:× 2 B5G5=85  
?5@2KE 24 G0A>2 ?>A;5 22545=8O A>AB02;O;> 0,5 % 4>7K A ?>?@02:>9 =0 <0AAC B5;0. >;8G5AB2>  
9>35:A>;0, ?>?040NI53> 2 >@30=87< @515=:0 2 B5G5=85 ?5@2KE 24 G0A>2 ?>A;5 22545=8O,

A>AB02;O5B B>;L:> 0,2 % 45BA:>9 4>7K.

5B8.

@5?0@0B ?@8<5=O5BAO 2 ?5480B@8G5A:>9 ?@0:B8:5.

A>1K5 <5@K 157>?0A=>AB8.

0: 8 2A5 A@54AB20 4;O ?0@5=B5@0;L=>3> 22545=8O, ?5@54 ?@8<5=5=85< "><>35:A>; A;54C5B 287C0;L=> ?@>25@8BL =0 >BACBAB285 =5@0AB2>@8=K ?@54=07=0G5=K B>;L:> 4;O >4=>@07>2>3> ?@8<5=5=8O. 58A?>;L7>20==K5 >AB0B:8 ?@5?0@0B0 =5>1E>48<> C=8GB>68BL.

A>15==>AB8 ?@8<5=5=8O.

1185 >A>15==>AB8 ?@8<5=5=8O =58>==KE <>=><5@=KE :>=B@0AB=KE A@54AB2.  
0;8G85 2 0=0<=575 0;;5@388, 0AB4A>45@60I85 :>=B@0AB=K5 ?@5?0@0BK B@51C5B ?>2KH5==>3> 2=8<0=8O. MB8E A;CG0OE =5>1E>48<> @0AA<>B@5BL 2>7<>6=>ABL ?@5<548:0F88 :>@B8:>AB5@>840<8 8;8 0=B03>=8AB0<8 H1- 8 H2- 38AB0<8=>2KE @5F5?B>@>2.  
8A: 2>7=8:=>25=8O BO65;KE ?>1>G=KE @50:F89 =0 "><>35:A>; >G5=L <0;. 4=0:> 9>4A>45@60I85 :>=B@0AB=K5 25I5AB20 <>3CB 2K7K20BL C3@>60NI85 687=8 D0B0;L=K5 0=0D8;0:B8G5A:85 /0=0D8;0:B>84=K5 @50:F88 8;8 4@C385 ?@>O2;5=8O 38?5@GC2AB28B5;L=>AB8. > MB>9 ?@8G8=5 A;54C5B 70@0=55 ?@54CA<>B@5BL ?>A;54>20B5;L=>ABL ;5G51=KE <5@>?@8OB89 2 A;CG05 2>7=8:=>25=8O A5@L57=KE ?>1>G=KE @50:F89 8 8<5BL 2 =0;8G88 =5>1E>481>@C4>20=85. >;6=0 1KBL ?>AB>O==0O :0=N;O 8;8 :0B5B5@ =0 2@52545=8O @5=B35=>:=B@0AB=>3> 8AA;54>20=8O A F5;LN >1;53G5=8O 1KAB@>3> 2=CB@825==>3> 22545=8O ;5:0@AB25==KE A@54AB2.  
# ?0F85=B>2, ?@8<5=ONI8E 15B0-04@5=>1;>;0B>@K, ?@>O2;5=8O 0=0D8;0:A88 <>3CB 1KBL 0B8?8G=K<8 8 >H81>G=> AG8B0BLAO 203CA=K<8 @50:F8O<8.  
> A@02=5=8N A 8>==K<8 ?@5?0@0B0<8 =58>==K5 :>=B@0AB=K5 A@54AB20 <5=LH5 2;8ONB in vitro =0 A8AB503C;OF88 :@>28. @8 ?@>2545=88 ?@>F54C@ A>AC48AB>9 :0B5B5@870F88 A;54C5B >G5=L BI0B5;L=> ?@845@6820BLAO <5B>48: 0=38>3@0D8G5A:8E 8AA;54>20=89 8 G0AB> ?@> 5@54 8 ?>A;5 22545=8O :>=B@0AB=>3> ?@5?0@0B0 =5>1E>48<> >15A?5G8BL 045:20B=>5 =0AKI5=85 >@30=87<0 >1A;54C5<>3> 684:>ABLN (384@0B0F8N). -B> 8<55B >A>1>5 7=0G5=85 4;O ?0F85=B>2 A <85;<=>9 1>;57=LN, A0E0@=K< 48015B><, =0@CH5=85< DC=:F88 ?>G5.; 0 B0:65 4;O <;045=F52, <0;5=L:8E 45B59 8 ?0F85=B>2 ?>68;>3> 2>7@0AB0.  
!;54C5B 1KBL 2=8<0B5;L=K< ?@8 8AA;54>20=88 ?0F85=B>2 A BO65;K<8 A5@45G=>-A>AC48ABK<8 701>;520=8O<8 8 ;53>G=>9 38?5@B5=7859 2 A2O78 A @8A:< @0728B8O 0@8B<88 8;8 =0@CH5=89 35 <>48=0<8:8.  
>;L=K5 A >AB@>9 F5@51@0;L=>9 ?0B>;>3859, >?CE>;O<8 <>730 8 M?8;5?A859 A;:>==K : @0728B8N AC4>@>3 8 B@51CNB >A>1>3> 2=8<0=8O. >2KH5==K9 @8A: @0728B8O AC4>@>3 8 =52@>;>38G5A:8E @50:F89 C 0;:>3>;8:>2 8 =0@:<0=>2. 54:> =01;N40;8AL A;CG08 2@5<5==>9 ?>B5@8 A;CE0 8;8 3;CE>BK ?>A;5 <85;>3@0D88, GB>, =025@=>5, A2O70=> A ?045=85< 402;5=8O A?8==> <>73>2>9 684:>AB8 2A;54AB285 ;N<10;L=>9 ?C=:F88.  
;O ?@54>B2@0I5=8O @0728B8O :>=B@0AB8=4CF8@>20==>9 =5D@>?0B88, =0@CH5=8O DC=:F89 ?>G5: 8;8 >AB@>9 ?>G5G=>9 =54>AB0B>G=>AB8, A2O70==>9 A 22545=85< :>=B@0AB=>3> 25I5AB20, =5>1E>48<0 >A>100 >AB>@>6=>ABL ?@8 8AA;54>20=88 1>;L=KE, :>B>@K5 C65 8<5NB =0@CH5=8O DC=:F89 ?>G5.; 8 1>;L=KE A0E0@=K< 48015B><, ?@8=04;560I8E : 3@C??5 @8A:0. "> 65 A0<>5 :0A05BAO 8 8AA;54>20=8O ?0F85=B>2 A ?0@0?@>B58=5<8O<8 (<85;<=>00 1>;57=L, <0:@>3;>1C;8=5<8O 0;L45=AB@5<0). !;54C5B A >AB>@>6=>ABLN ?@8<5=OBL 9>4A>45@60I85 :>=B@0AB=K5 A@54AB20 1>;L=K< A D5>E@><>F8B><>9 8;8 ?0F85=B0<, ?@8=04;560I8< : 3@C??5 @8A:0.  
5@K ?@54>B2@0I5=8O ?>1>G=KE @50:F89:  
CAB0=>2;5=85 ?0F85=B>2, ?@8=04;560I8E : 3@C??5 @8A:0;  
>15A?5G5=85 045:20B=>9 384@0B0F88; 5A;8 =5>1E>48<>, MB> <>65B 1KBL 4>AB83=CB> A ?<>ILN ?>AB>O==>9 2=CB@825==>9 8=DC788, :>B>@CN =0G8=0NB 5I5 4> <<<5=B0 22545=8O :>=B@0AB=>3> ?@5?0@0B0 8 ?@>4>;60NB 4> <<<5=B0 53> 2K2545=8O ?>G:0<8; ?@54>B2@0I5=85 4>?>;=8B5;L=>9 =03@C7:8 =0 ?>G:8, 2>7=8:0NI59 ?@8 ?@8<5=5=88 =5D@>B>:A8G5A:8E ?@5?0@0B>2, A@54AB2 4;O ?5@>@0;L=>9 E>;5F8AB>3@0D88, ?@8 ?5@560B88 ?>G5G=KE 0@B5@89, 0=38>?;0AB8:8 ?>G5G=KE 0@B5@89, E8@C@38G5A:8E >?5@0F8OE, 4> 2K2545=8O :>=B@0AB=>3> 25I5AB20 87 >@30=87<0;

?>2B>@=K5 @5=B35=>:=B@0AB=K5 8AA;54>20=8O =C6=> ?@>2>48BL ?>A;5 ?>:=9 =>@<0;870F88  
DC=:F89 ?>G5: ?>A;5 ?>A;54=53> 22545=8O ?@5?0@0B0.  
0F85=BK A A0E0@=K< 48015B><, :>B>@K5 ?@8<5=ONB B5@0?8N <5BD>@<8=>@8<5=5=85  
9>4A>45@60I8E :>=B@0AB=KE 25I5AB2 1>;L=K< A0E0@=K< 48015B><, :>B>@K5 ?@8=8<ONB  
<5BD>@<8=, >A>15=> ?0F85=B0< A =0@CH5=85< DC=:F89 ?>G5:, <>65B ?@82>48BL : ;0:B>0F84>7C.  
;O ?@54C?@5645=8O ;0:B>F84>70 C ?0F85=B>2 A A0E0@=K< 48015B><, :>B>@K5 ?@8<5=ONB  
B5@0?8N <5BD>@<8=><, ?5@54 2=CB@8A>AC48ABK< 22545=85< :>=B@0AB=>3> A@54AB20,  
A>45@60I53> 9>4, =5>1E>48<> 87<5@8BL C@>25=L :@50B8=8=0 AK2>@>B:8 :@>28 8 ?@8=OBL  
?@54C?@548B5;L=K5 <5@K 2 =865C:070==KE A;CG0OE.  
>@<0;L=K9 C@>25=L :@50B8=8=0 AK2>@>B:8 :@>28 (<130 . @85< <5BD>@<8=0 A;54C5B  
?@5:@0B8BL 2> 2@5=B@0AB=>3> A@54AB20 8 =5 2>7>1=>2;OBL 2 B5G5=85 48 G0A>2 8;8 4>  
2>AAB0=>2;5=8O DC=:F89 ?>G5:/:@50B8=8=0 AK2>@>B:8 :@>28 4> =>@<0;L=>3> C@>2=O.  
>2KH5=85 C@>2=O :@50B8=8=0 AK2>@>B:8 :@>28 (>130 . !;54C5B ?@5:@0B8BL ?@85< <5BD>@  
<8=0 8 >B;>68BL >1A;54>20=85 :>=B@0AB=K< A@54AB2>< =0  
48 G0A>2. "5@0?8N <5BD>@<8=>< 2>7>1=>2;ONB B>;L:> 2 A;CG05, 5A;8 DC=:F88 ?>G5:/:@50B8=8=0  
AK2>@>B:8 :@>28 >AB0NBAO =57<5=5==K<8. =5>B;>6=KE A;CG0OE, ?@8 :>B>@KE >B<5G05BAO  
=0@CH5=85 DC=:F89 ?>G5: 8;8 A>AB>O=85 8E =58725AB=>, 2@0G 4>;65= >F5=8BL A>>B=>H5=85  
@8A:/?>;L70 4;O ?0F85=B0 >B ?@8<5=5=8O ?@5?0@0B0 8 ?@8=OBL <5@K ?@54>AB>@>6=>AB8:  
?@5:@0B8BL ?@85< <5BD>@<8=0. A>15=>=> 206=> >15A?5G5=85 045:20B=>9 384@0B0F88 ?0F85=B>2  
?5@54 8 2 B5G5=85 24 G0A>2 ?>A;5 22545=8O :>=B@0AB=>3> A@54AB20. !;54C5B :>=B@>;8@>20BL  
DC=:F8N ?>G5: (2 G0AB=>AB8, :@50B8=8= AK2>@>B:8), C@>25=L <>;>G=>9 :8A;>BK 2 AK2>@>B:5  
:@>28 8 pH :@>28.  
!CI5AB2C5B ?>B5=F80;L=K9 @8A: @0728B8O ?5G5=>G=>9 =54>AB0B>G=>AB8. A>15=>=>  
>AB>@>6=K<8 A;54C5B 1KBL A 1>;L=K<8 A BO65;K<8 :<18=8@>20==K<8 =0@CH5=8O<8 DC=:F89  
?>G5: 8 ?5G5=8, ?>A:>;L:C C 40==>9 3@C??K ?0F85=B>2 =01;N405BAO 7=0G8B5;L=>5 A=865=85  
::8@5=A0 :>=B@0AB=KE 25I5AB2. 0F85=BK =0 35<>480;875 <>3CB ?>;CG0BL :>=B@0AB=>5  
25I5AB2> 4;O @048>;>38G5A:8E ?@>F54C@.  
5B =5>1E>48<>AB8 :>@>5;OF88 2@5<5=8 <564C 8=J5:F859 :>=B@0AB=>3> 25I5AB20 8 A50=A< 35  
<>480;870, ?>A:>;L:C =5B =8:0:8E 4>:070B5;LAB2 B>3>, GB> 35<>480;87 ?@54>B2@0I05B @0728B85  
:>=B@0AB8=4CF8@>20==>9 =5D@>?0B88 C ?0F85=B>2 A =0@CH5=85< DC=:F89 ?>G5:.  
@8<5=5=85 9>4A>45@60I8E @5=B35=>:=B@0AB=KE 25I5AB2 <>65B CA8;820BL A8;L=KE A  
<=>3>C7;>2K< 7>1<< ?>A;5 22545=8O 9>4A>45@60I8E :>=B@0AB=KE A@54AB2 ACI5AB2C5B @8A:  
@0728B8O 38?5@B8@5>8487<0.  
KE>4 :>=B@0AB=>3> A@54AB20 87 A>AC4>2 @54:> A>?@>2>640;AO<5AB=>9 1>;LN 8 >B5:<<,  
?@>E>40I8< 157 ?>A;54AB289. 4=0:> 70D8:A8@>20=K A;CG08 2>A?0;5=8O 8 =5:@>70 B:0=59. 0: >1I85  
<5@K @5:><5=4C5BAO ?> 2>7<>6=>AB8 ?>4J5< 8 >E;0645=85 <5AB0 22545=8O 8=J5:F88. A;CG05  
@0728B8O :<<0 2>7<>6=> ?@>2545=85 E8@C@38G5A:>9 45:>  
01;N45=85 70 ?0F85=B> >A;5 22545=8O :>=B@0AB=>3> ?@5?0@0B0 A;54C5B =01;N40BL 70  
A>AB>O=85< ?0F85=B0 2 B5G5=85 :0: <8=8  
=B@0B5:0;L=>5 22545=85. >A;5 ?@>2545=8O <85;>3@0D88 ?0F85=B 4>;65= =0E>48BLAO 2 ?>:>5 =5  
<5=55 1 G0A0, ;560 A ?>4=OB>9 =0 20° 3>;>2>9 8 3@C4=>9 ;;5B:>9. >A;5 MB>3> 1>;L=>3><>6=>  
?5@52>48BL =0 0<1C;0B>@=K9 @568<, >4=0:> ?0F85=B 4>;65= 871530BL =0;:>=>2. @8 A>1;N45=88  
?>AB5;L=>3> @568<0 ?>4=OB>5 ?>;>65=85 3>;>2K 8 3@C48 4>;6=> A>E@0=OBLAO 2 B5G5=85  
?5@2KE  
6 G0A>2. @8 ?>4>7@5=88 =0 =87:89 ?>@>3 @0728B8O AC4>@>3 =5>1E>48<> =01;N40BL 70 8AA;54C5  
A>15=>=>AB8 ?@8<5=5=8O 45BO!;54C5B ?><=8BL > 2>7<>6=>AB8 @0728B8O B@0=78B>@=>3>  
38?>B8@5>8487<0 C =54=>=>H5==KE, =>2>@>645==KE 8 4@C38E 45B59 2 A2O78 A 22545=85<  
9>4A>45@60I8E :>=B@0AB=KE 25I5AB2. 54=>=>H5==K5 45B8 8<5NB ?>2KH5==CN  
GC2AB28B5;L=>ABL : 9>4C. 5>1E>48<> :>=B@>;8@>20BL DC=:F8N I8B>284=>9 65;57K. @8 ?@8  
<5=5=88 9>4A>45@60I8E :>=B@0AB=KE 25I5AB2 15@5<5==K< 65=18=0< A;54C5B :>=B@>;8@>20BL  
DC=:F8N I8B>284=>9 65;57K C =>2>@>645==KE 2 B5G5=85 ?5@2>9 =545;8 687=8.  
A>15=>=> <;045=F0< 4> 8 ?>A;5 22545=8O :>=B@0AB=>3> ?@5?0@0B0 =5>1E>48<> >15A?5G8BL  
045:20B=CN 384@0B0F8N. 5G5=85 =5D@>B>:A8G=>AB8 4>;6=> 1KBL 2725H5==K  
# 45B59 4> 1 3>40 8 >A>15=>=> C =>2>@>645==KE =0@CH5=85 35<>48=0<8:8 8 M;5:B@>;8B=>3>  
10;0=A0 ?@>8AE>48B >A>15=>=> ;53:>.



-B> ;5:0@AB25==>5 A@54AB2> A>45@68B<5=55 1 <<>;L//4>7C =0B@8O, B> 5ABL ?@0:B8G5A:8  
A2>1>4=> >B =0B@8O.

!>A>1=>ABL 2;8OBL =0 A:>@>ABL @50:F88 ?@8 C?@02;5=88 02B>B@0=A?>@B< 8;8 @01>B5 A  
4@C38<8 <5E0=87<0<8.

8:0:8E 8AA;54>20=89 2;8O=8O ?@5?0@0B0 =0 A?>A>1=>ABL C?@02;OBL 02B>B@0=A?>@B< 8  
@01>B0BL A<5E0=87<0<8 =5 ?@>2>48;>AL. 5 @5:><5=4C5BAO C?@02;OBL 02B>B@0=A?>@B< 8  
@01>B0BL A> A;>6=>9 B5E=8:>9 =0 ?@>BO65=88 ?5@2KE 24 G0A>2 ?>A;5 8=B@0B5:0;L=>3>  
22545=8O :>=B@0AB=KE A@54AB2. @8 =0;8G88 A8<2 ?>A;5 ?@>2545=8O <85;>3@0D88 @5H5=85  
=C6=> ?@8=8<0BL 8=48284C0;L=>.

708<>459AB285 A 4@C38<8 ;5:0@AB25==K<8 A@54AB20<8 8 4@C385 284K 2708<>459AB289.

@8<5=5=85 9>4A>45@60I8E :=B@0AB=KE 25I5AB2 1>;L=K< A0E0@=K< 48015B><, ?@8=8<0NI8<  
<5BD>@<8=, <>65B ?@825AB8 :>1@0B8<>G5: 8 ;0:B>0F84>7C (A15==>AB8 ?@8<5=5=8O»).  
0F85=BK, :>B>@K5 ?@8=8<0;8 <5=55 G5< 70 2 =545;8 4> 8AA;54>20=8O 8=B5@;59:8=-2, 8<5NB  
A:;>=>ABL :>B40;Q==K< ?>1>G=K< @50:F8O< (3@8??>?>4>1=>5 A>AB>O=85 8;8 :>6=K5 @50:F88).  
A5 9>4A>45@60I85 :=B@0AB=K5 25I5AB20 <>3CB 2708<>459AB2>20BL A 4803=>AB8G5A:8<8  
B5AB0<8 8AA;54>20=89 DC=:F89 I8B>284=>9 65;57K, ?>MB>A>1=>ABL I8B>284=>9 65;57K  
A2O7K20BL 9>4 <>65B A=860BLAO =0 ?5@8>4 4> =5A:>;L:8E =545;L.  
KA>:0O :=F5=B@0F8O :=B@0AB=KE A@54AB2 2 AK2>@>B:5 :@>28 8 <>G5 <>65B 2;8OBL =0  
@57C;LB0BK ;01>@0B>@=KE ?>.070B5;59 18;8@C18=0, 15;>2 8 =5>@30=8G5A:8E A>548=5=89  
(=0?@8<5@, 65;570, <548, :0;LF8O, D>AD0B>2), ?>MB>@0B>@=K5 0=0;87K =5 A;54C5B ?@>2>48BL 2  
B>B 65 45=L.

\$0@<0:>;>38G5A:85 A2>9AB20.

\$0@<0:>48=0<8:0.

>35:A>; =58>==>5, <=><5@=>5, B@89>48@>20==>5, 2>4>@0AB2>@8<>5 @5=B35=>:=B@0AB=>5  
A@54AB2>.

@8 8AA;54>20=88 74>@>2KE 4>1@>2>;LF52 ?>A;5 2=CB@825==>9 8=J5:F88 9>35:A>;0 =5 1K;>  
CAB0=>2;5=> 7=0G8B;>:=5=89 1>;LH8=AB20 ?>.070B5;59 35<>48=0<8:8, ;8=8:>-18>E8<8G5A:8E  
?>.070B5;59 8 ?>.070B5;59 :>03C;OF88. 7<5=5=8O =5:>B>@KE ;01>@0B>@=KE ?>.070B5;59 1K;8  
=57=0G8B5;L=K<8 8 =5 AG8B0NBAO ;;8=8G5A:8 7=0G8

\$0@<0:>:8=5B8:0.

@81;878B5;L=> 100 % 22545==>3> 2=CB@825==>9 >35:A>;0 2K45;O5BAO 2 =587<5=5==>< 2845 G5@57  
=>@<0;L=> DC=:F8>=8@CNI85 ?>G:8 =0 ?@>BO65=88 24 G0A>2. 5@8>4 ?>;C2K2545=8O ?@5?0@0B0  
C ?0F85=B>2 A =>@<0;L=>9 DC=:F859 ?>G5: A>AB02;O5B 2 G0A0. 5B01>;8BK ?@5?0@0B0 =5  
CAB0=>2;5=K. !2O7K20=85 9>35:A>;0 A 15;:0<8 ?;07

\$0@<0F52B8G5A:85 E0@0:B5@8AB8:8.

A=>2=K5 D878:>-E8<8G5A:85 A2>9AB20: ?@>7@0G=0O 15AF25B=0O 8;8 A25B;>-65;B>3> F25B0  
684:>ABL (@0AB2>@).

!@>: 3>4=>AB8. 3 3>40.

5 ?@8<5=OBL ?>A;5 >:=G0=8O A@>:0 3>4=>AB8, C:070==>3> =0 C?0:>2:5.

#A;>28O E@0=5=8O.

%@0=8BL 2 >@838=0;L=>9 C?0:>2:5 2 70I8I5==>< >B 2B>@8G=>3> @5=B35=>2A:>3> 87;CG5=8O  
<5AB5 ?@8 B5°!. %@0=8BL 2 =54>ABC?=>< 4;O 45B59 <5AB5.

#?0:>2:0.

> 20 <; 2 0 5 05.

> 20 <; 8;8 50 <;, 8;8 100 <; 2> D;0:>=5. > 1 D;0:>=C 2 ?0G:5.

0B53>@8O >B?CA:0. > @5F5?BC.

@>872>48B5;L.

<<\$0@<0:».

5AB>=0E>645=85.

#: @08=0, 04080, 3. 852, C;. \$@C=75, 63.