

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

®
(!OZAAR®)

!;:04:

4VNG0 @5G>28=0: losartan potassium;
1 B01;5B:0, 2:@8B0 >1>;>=:>N, 100 <3 ;>70@B0=C :0;VN;
4>?>28=8: F5;N;>70 :@8AB0;VG=0, ;0:B>78 <=>3V4@0B, :@>E<0;L ?@565;0B8=V7>20=89 1500,
<03=VN AB50@0B 4@V1=89 ?>@>H>;;
>1>;>=:0: 3V4@>:A8?@>?V;F5;N;>70, 3V?@><5;>70, B8B0=C 4V>:A84 (171), 2VA: :0@=0C1AL:89.

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. @>ABV ?@5?0@0B8 0=B03>=VABV2 @5F5?B>@V2 0=3V>B5=78=C
II.

>4 " ! !09! 01.

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

>:070==O.

□ V:C20==O 5A5=FW0;L=>W 3V?5@B5=7VW C 4>@>A;8E, 0 B0:>6 4VB59 V ?V4;VB:V2 2V:× 2V4 6
4> 18 @>:V2.

□ V:C20==O 70E2>@N20==O =8@>: C 4>@>A;8E ?0FVT=BV2 V7 3V?5@B5=7VTN V FC:@>28<
4V015B>< B8?C 7 ?@>B5W=C@VTN ≥ 0,5 3/4>1C O: G0AB8=0 0=B83V?5@B5=782=>W B5@0?VW.

□ V:C20==O E@>=VG=>W A5@F52>W =54>AB0B=>ABV (C ?0FVT=BV2 2V:× 60 @>:V2 B0 AB0@H5),
>:;8 70AB>AC20==O V=3V1VB>@V2 0=3V>B5=78=?5@5B2>@N20;L=>3> D5@<5=BC (\$) 22060TBLAO
=5<>6;828< 7 ?@8G8=8 =5ACABV, >A>1;82> ?@8 :0H;V, 01> ?@>B8?>:070=5. 0FVT=BV2 V7 A5@F52>N
=54>AB0B=VABN, AB0= O:8E AB01V;V7C202AO ?@8 70AB>AC20==V V=3V1VB>@0 \$, =5 A;V4
?5@52>48B8 =0 ;V:C20==O ;>70@B0=>3> H;C=>G:0 <0T AB0=>28B8 ≤ 40 %, AB0=<0T 1CB8 ;;V=VG=>
AB01V;L=8<, B0:>6 ?0FVT=B>2V A;V4 4>B@82;5=>3> @5684> E@>=VG=>W A5@F52>W
=54>AB0B=>ABV.

□ =865==O @878:C @>728B:C V=AC;LBC C 4>@>A;8E ?0FVT=BV2 7 0@B5@V0;L=>N
3V?5@B5=7VTN V 3V?5@B@>DVTN ;V2>3> H;C=>G:0, I> ?V4B25@465=> .

@>B8?>:070==O.

- V?5@GCB;82VABL 4> 4VNG>W @5G>28=8 B0 4> 1C4L-O:>W 4>?>W @5G>28=8, I> 2E>48BL 4>
A;:04C ?@5?0@0BC;
- "O6:V ?>@CH5==O DC=:FWW ?5GV=:8;
- 03VB=V 01> 6V=:8, O:V ?;0=CNBL 70203VB=VB8 (482. @>74V; «0AB>AC20==O C ?5@V>4
203VB=>ABV 01> 3>4C20==O 3@C44N»;

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

"01;5B:8 >700@® <>6=0 70AB>A>2C20B8 =570;56=> 2V4 ?@89>1 A;:O=:>N 2>48.

@B5@V0;L=0 3V?5@B5=7VO

0728G09 ?>G0B:>20 V ?V4B@870 4;O 1V;LH>ABV E2>@8E AB0=>28BL50 <3 ?@5?0@0BC 1 @07 =0
4>1C (1 B01;5B:0 >700@C® 50 <3). 0:A8<0;L=89 0=B83V?5@B5=782=89 5D5:B 4>AO30TBLAO =0
3-6 B8645=L 2V4 ?>G0B:C ;V:C20==O >700@> 100 <3 1 @07 =0 4>1C (2@0=FW).

@5?0@0B <>6=0 70AB>A>2C20B8 C ?>T4=0==V 7 V=H8<8 0=B83V?5@B5=782=8<8 ?@5?0@0B0<8,
>A>1;82> 7 4VC@5B8:0<8 (=0?@8;:04, 3V4@>E;>@>BV0784><).

0FVT=B8 7 3V?5@B5=7VTN B0 FC:@>28< 4V015B>< B8?C (?@>B5W=C@VO ≥ 0,5 3/4>1C)

0728G09 ?>G0B:>20 4>70 AB0=>28BL 50 <3 (1 B01;5B:0 >700@C® 50 <3) 1 @07 =0 4>1C. >7C <>6=0
71V;LH8B8 4> 100 <3 1 @07 =0 4>1C 70;56=> 2V4 B>3>, O:8<8 T ?>:07=8:8 0@B5@V0;L=>3> B8A:C
G5@57 1 G0B:C ;V:C20==O.>700@® <>6=0 70AB>A>2C20B8 7 V=H8<8 0=B83V?5@B5=782=8<8
?@5?0@0B0<8 (=0?@8:;04, 4VC@5B8:0<8, 1;>:0B>@0<8 :0;LFV28E :0=0;V2, 1;>:0B>@0<8 α- 01>
β-@5F5?B>@V2, ?@5?0@0B0<8 F5=B@0;L=>W 4VW), 0 B0:>6 7 V=AC;V=< B0 V=H8<8 3V?>3;V:5
!5@F520 =54>AB0B=VABL.

0728G09 ?>G0B:>20 4>70 ;>70@B0=C 4;O ?0FVT=BV2 V7 E@>=VG=>N A5@F52>N =54>AB0B=VABN
AB0=>28BL 12,5 <3 1 @07 =0 4>1C. /: ?@028;>, 4>70 B8B@CTBLAO 7 B86=528< V=B5@20;< (B>1B>
12,5 <3 =0 4>1C, 25 <3 =0 4>1C, 50 <3 =0 4>1C) 4> 728G09=>W ?V4B@8W 4>78 50 <3 (1 B01;5B:0
>700@C® 50 <3) 1 @07 =0 4>1C 70;56=> 2V4 V=482V4C0;L=>W ?5@5=>A8<>ABV.
<5=H5==O @878:C @>728B:C V=AC;LBC C ?0FVT=BV2 7 0@B5@V0;L=>N 3V?5@B5=7VTN V
3V?5@B@>DVTN ;V2>3> H;C=>G:0, ?V4B25@465=>N =0.

0728G09 ?>G0B:>20 4>70 AB0=>28BL 50 <3 >700@C® (1 B01;5B:0 >700@C® 50 <3) 1 @07 =0 4>1C.
0;56=> 2V4 73> B8A:C 4> ;V:C20==O A;V4 4>40B8 3V4@>E;@>BV0784 C =87L;V9 4>7V B0/01>
71V;LH8B8 4>7C >700@C® 4> 100 <3 1 @07 =0 4>1C.

:@5
0AB>AC20==O ?0FVT=B0< 7V 7=865=8< >1'T<>< F8@:C;NNG>W :@>2V.
0FVT=B0< 7V 7=865=8< >1'T<>< F8@:C;NNG>W :@>2V (=0?@8:;04, C=0A;V4> ;V:C20==O 28A>:8<8
4>70<8 4VC@5B8:V2) @>7?>G8=0B8 B5@0?VN =5>1EV4=> 7 4>78 25 <3 1 @07 =0 4>1C.

0AB>AC20==O ?0FVT=B0< V7 ?>@CH5==O< DC=:FVW =8@>: B0 C ?0FVT=BV2, O:8< ?@>2>4OBL
35<>4V0;V7.

@8 ?@87=0G5==V >700@C® ?0FVT=B0< V7 ?>@CH5==O< DC=:FVW =8@>:, 0 B0:>6 ?0FVT=B0<, O:8
< ?@>2>4OBL 35<>4V0;V7, ?>G0B:>2C :>@5:FVN 4>78 ?@>2>48B8 =5 ?>B@V1=>.

0AB>AC20==O ?0FVT=B0< 7 ?>@CH5==O< DC=:FVW ?5GV=:8.

;O ?0FVT=BV2 V7 ?>@CH5==O< DC=:FVW ?5GV=:8 2 0=0<=57V A;V4 @>73;O=CB8 ?8B0==O I>4>
?@87=0G5==O ?@5?0@0BC C <5=HV9 4>7V. 5<0T 4>A2V4C ;V:C20==O ?0FVT=BV2 V7 B06:8<8
?>@CH5==O<8 DC=:FVW ?5GV=:8, B>70@B0= ?@>B8?>:070=89 FV9 3@C?V ?0FVT=BV2.

0AB>AC20==O 4VBO<.

0=V I>4> 5D5:B82=>ABV B0 157?5:8 70AB>AC20==O ;>70@B0=C 4VBO< B0 ?V4;VB:0< 2V:< 6-
18@>:V2 4;O ;V:C20==O 0@B5@V0;L=>W 3V?5@B5=7VW >1<565=V. "0:>6 T<0;> 40=8E I>4> D0@
<0:>:V=5B8:8 C 4VB59 7 0@B5@V0;L=>N 3V?5@B5=7VTN 2V:< AB0@H5 1

;O 4VB59, O:V <>6CBL :>2B0B8 B01;5B:8, V 2 O:8E <0A0 BV;0 1V;LH5 20 :3 B0<5=H5 50 :3, @5:>
<5=4>20=0 4>70 AB0=>28BL 25 <3 1 @07 =0 4>1C. # 28=OB:>28E 28?04:0E 4>7C <>6=0 71V;LH8B8 4>
<0:A8<0;L=>W 50 <3 1 @07 =0 4>1C. >7C A;V4 :>@83C20B8 70;56=> 2V4 2?;82C =0 @V25=L
0@B5@V0;L=>3> B8A:C.

?0FVT=BV2 7 <0A>N BV;0 ?>=04 50 :3 70728G09 @07>20 4>70 AB0=>28BL 50 <3 1 @07 =0 4>1C. #
28=OB:>28E 28?04:0E 4>7C <>6=0 71V;LH8B8 4> <0:A8<0;L=>W 100 <3 1 @07 =0 4>1C. 0AB>AC20==O
4>7, I> ?5@528ICNBL 1,4 <3/:3 (01> 1V;LH5 100 <3) =0 4>1C, C 4VB59 =5 282G0;>AO.

>70@B0= =5 @5:><5=4>20=89 4;O 70AB>AC20==O 4VBO< 2V:< <>4H5 6 @>:V2, >A;V;L:8 40=8E
I>4> 70AB>AC20==O ?@5?0@0BC C FV9 3@C?V ?0FVT=BV2 =54>AB0B=L>.

@5?0@0B =5 @5:><5=4CTBLAO 70AB>A>2C20B8 4VBO< 7V H284:VABN ;:C1>G:>2>W
DV;LB@0FVW

< 30 <;E2/1,73<2, >A:V;L:8 =5<0T 2V4?>2V4=8E 40=8E I>4> 70AB>AC20==O.

>70@B0= B0:>6 =5 @5:><5=4CTBLAO 4;O 70AB>AC20==O 4VBO< V7 ?>@CH5==O< DC=:FVW
?5GV=:8.

0AB>AC20==O ?0FVT=B0< ;VB=L>3> 2V:C.

/: ?@028;>, =5<0T ?>B@518 C :>@83C20==V ?>G0B:>2>W 4>78 4;O ?0FVT=BV2 ;VB=L>3> 2V:C, E>G0
A;V4 2@0E>2C20B8 <>6;82VABL ?@87=0G5==O ?@5?0@0BC C ?>G0B:>2V9 4>7V 25<3 4;O
?0FVT=BV2 2V:< AB0@H5 75 @>:V2.

>1VG=V @50:FVW.

>1VG=>N @50:FVTN, ?@> O:C =09G0ABVH5 ?>2V4><;O;>AO C ;V=VG=8E 4>A;V465==OE, 1C;> 70?0
<>@>G5==O.

'0AB>B0 ?>1VG=8E @50:FV9, 2:070=8E =86G5, 287=0G5=0 O: =0ABC?=0: 4C65 G0AB>: ≥1/10; G0AB>:
2V4 ≥1/100 4> <1/10; =5G0AB>: 2V4 ≥1/1000 4> <1/100; @V4:>: 2V4 ≥1/10000 4> <1/1000; 4C65 @V4:>:
<1/10000; =52V4><> (=5<>6;82> 287=0G8B8 70 VA=CNG8<8 40=8<8).

@B5@V0;L=0 3V?5@B5=7VO.

:=B@>;L>20=8E ::V=VG=8E 4>A;V465==OE, 45 3 300 4>@>A;8E ?0FVT=BV2 7 5A5=FV0;L=>N 3V?5@B5=7VTN 2V:< 18 @>:V2 B0 AB0@H5 70AB>A>2C20;8 ;>70@B0=, ?>2V4<;O;>AO ?@> =0ABC?=V ?>1VG=V @50:FVW.

I>:C =5@2>2>W A8AB5<8: G0AB> 70?0<>@>G5==O, 25@B83>; =5G0AB> A>=;82VABL, 3>;>2=89 1V;L, 157A>==O, <'O7>2V AC4<8.

I>:C A5@FO: =5G0AB> ?0;L?VB0FVO, AB5=>:0@4VO, B0EV:0@4VO.

I>:C AC48==>W A8AB5<8: =5G0AB> A8<0B8G=0 3V?>B5=7VO (>A>1;82> C ?0FVT=BV2 7 2=CB@VH=L>AC48==>N 453V4@0B0FVTN, =0?@8::04, ?0FVT=B8 7 BO6:>N A5@F52>N =54>AB0B=VABN 01> ?@8 ;V:C20==V 4VC@5B8:0<8 C 28A>:8E 4>70E), 4>7>70;56=89 >@B>AB0B8G=89 5D5:B, 28A8?.

I>:C B@02=>3> B@0:BC: =5G0AB> 014>@.

I>:C @5A?V@0B>@=>W A8AB5<8: :0H5;L, =568BL, A8=CA8B, D0@8=3VB, V=D5:FVO 25@E=VE 48E0;L=8E H;OEV2.

030;L=89 AB0= B0 ?>@CH5==O, ?>2O70=V 7V A?>A>I>< 70AB>AC20==O ?@5?0@0BC: =5G0AB> 0AB5=VO, A;01:VABL, =01@O:8.

01>@0B>@=V ?>:07=8:8. # :=B@>;L>20=8E ::V=VG=8E 4>A;V465==OE ::V=VG=> 7=0GCIV 7 @0B>@=8E ?>:07=8:V2 @V4:> 1C;8 ?>2O70=V V7 70AB>AC20==O< B01;5B>; ;>70@B0=C. V25=L " ?V428IC202AO @V4:> V 70728G09 =>@<0;V7C202AO ?VA;O ?@8?8=5==O 70AB>AC20==O ?@5?0@0BC. V?5@:0;VT20BFV :@>2V > 5,5 <<>;L;) A?>AB5@V30;0AO C 1,5 % ?0FVT=BV2 7 0@B5@V0;L=>N 3V?5@B5=7VTN.

0FVT=B8 7 3V?5@B@>DVTN ;V2>3> H;C=>G:0 A5@FO.

:=B@>;L>20=>A;V465==V, 45 ?@89<0;8 CG0ABL 9 193 ?0FVT=BV2 V7 3V?5@B@>DVTN ;V2>3> H;C=>G:0, 2V:< 2V4 55 4> 80 @>:V2, ?>2V4<;O;>AO ?@> =0ABC?=V ?>1VG=V @50:FVW.

I>:C =5@2>2>W A8AB5<8: G0AB> 70?0<>@>G5==O.

I>:C >@30=0 A;CEC B0 ;01V@8=BC: G0AB> 25@B83>.

030;L=89 AB0= B0 ?>@CH5==O, ?>2O70=V 7V A?>A>I>< 70AB>AC20==O ?@5?0@0BC: G0AB> 0AB5=VO/A;01:VABL.

%@>=VG=0 A5@F520 =54>AB0B=VABL

:=B@>;L>20=>A;V465==V, 45 ?@89<0;8 CG0ABL ?@81;87=> 3 900 ?0FVT=BV2 V7 A5@F52>N =54>AB0B=VABN 2V:< 20 @>:V2 V AB0@HV, ?>2V4<;O;>AO ?@> =0ABC?=V ?>1VG=V @50:FVW.

I>:C =5@2>2>W A8AB5<8: =5G0AB> 70?0<>@>G5==O, 3>;>2=89 1V;L; @V4:> ?0@5AB57VO.

I>:C A5@FO: @V4:> A8=>?5, DV1@8;OFVO ?5@54A5@4L, V=AC;LB.

I>:C AC48==>W A8AB5<8: =5G0AB> 0@B5@V0;L=0 3V?>B5=7VO, 2;;NG0NG8 >@B>AB0B8G=C 3V?>B5=7VN.

I>:C @5A?V@0B>@=>3> B@0:BC, >@30=V2 3@C4=>W ;;VB:8 B0 A5@54>ABV==O: =5G0AB> 48A?=>5.

I>:C B@02=>3> B@0:BC: =5G0AB> 4V0@5O, =C4>B0, 1;N20==O.

I>:C H:V@8 B0 ?V4H:V@=>W ;;VB:>28=8: =5G0AB> :@>?82O=:0, A25@1V6, 28A8?.

030;L=89 AB0= B0 ?>@CH5==O, ?>2O70=V 7V A?>A>I>< 70AB>AC20==O ?@5?0@0BC: =5G0AB> 0AB5=VO/A;01:VABL.

01>@0B>@=V ?>:07=8:8: =5G0AB> ?V428I5==O @V2=O A5G>28=8 :@>2V, :@50B8=V=C C A8@>20BFV :@>2V B0 :0;VN C A8@>20BFV :@>2V.

@B5@V0;L=0 3V?5@B5=7VO V FC:@>289 4V015B B8?C , I> AC?@>2>46CTBLAO 70E2>@N20==O< =8@>:.

:=B@>;L>20=>A;V465==V, 45 ?@89<0;8 CG0ABL 1 513 ?0FVT=BV2 V7 FC:@>28< 4V015B<< B8?C B0 ?@>B5W=C@VTN 2V:< AB0@H5 31 @>:C, ?>2V4<;O;>AO ?@> =0ABC?=V ?>1VG=V @50:FVW, ?>2O70=V V7 70AB>AC20==O< ;070@B0=C.

I>:C =5@2>2>W A8AB5<8: G0AB> 70?0<>@>G5==O.

I>:C AC48==>W A8AB5<8: G0AB> 0@B5@V0;L=0 3V?>B5=7VO.

030;L=89 AB0= B0 ?>@CH5==O, ?>2O70=V 7V A?>A>I>< 70AB>AC20==O ?@5?0@0BC: G0AB> 0AB5=VO/A;01:VABL.

01>@0B>@=V ?>:07=8:8: G0AB> 3V?>3;V:5

0ABC?=V ?>1VG=V @50:FVW 28=8:0;8 G0ABVH5 C ?0FVT=BV2, O:V 70AB>A>2C20;8 ;>70@B0=, =V6 C ?0FVT=BV2 3@C?8 ?;0F51>.

I>:C A8AB5<8 :@>2V B0 ;VW A8AB5<8: 0=5
I>:C A5@FO: A8=>?5, ?0;L?VB0FVO.
I>:C AC48==>W A8AB5<8: >@B>AB0B8G=0 3V?>B5=7VO.
I>:C B@02=>3> B@0:BC: 4V0@5O.
I>:C A:5;5B=>-<O7>2>W A8AB5<8 B0 A?>;CG=>W B:0=8=8: 1V;L C A?8=V.
I>:C =8@>: B0 A5G>282V4=8E H;OEV2: V=D5:FVW A5G>282V4=8E H;OEV2.
030;L=89 AB0= B0 ?>@CH5==O, ?>2O70=V 7V A?>A>I>< 70AB>AC20==O ?@5?0@0BC:
3@8?>?>4V1=V A8<8.
01>@0B>@=V ?>:07=8:8. # ;;V=VG=>A;V465==V 70 CG0ABN ?0FVT=BV2 V7 FC:@>28< 4V015B<<
B8?C V =5D@>?0BVTN C 9,9 % ?0FVT=BV2, O:V >B@8 B01;5B:8 ;>70@B0=C, 28=8;;0 3V?5@:0;VT
> 5,5 <:2/; V C 3,4 % ?0FVT=BV2 3@C?8 ?;0F51>.
>AB<0@:5B8=3>25 A?>AB5@565==O.
@>B03<< ?>AB<0@:5B8=3>2>3> A?>AB5@565==O ?>2V4<<;O;>AO ?@> =0ABC?=V ?>1VG=V
@50:FVW.
I>:C A8AB5<8 :@>2V V ;VW A8AB5<8: 0=5<1>F8B>?5=VO.
I>:C >@30=0 A;CEC B0 ;01V@8=BC: 472V= C 2CE0E.
I>:C VW A8AB5<8: @V4:> @50:FVW 3V?5@GCB;82>ABV (0=0DV;0:B8G=V @50:FVW,
0=3V>=52@>B8G=89 =01@O:, 2;;NG0NG8 =01@O: 3>@B0=V B0 3>;>A>2>W IV;8=8, I> ?@872>48BL
4> >1AB@C:FVW 48E0;L=8E H;OEV2 B0/01> =01@O:8 >1;8GGO, 3C1, 3;>B:8 V/01> O78:0); C 45O:8E
?0FVT=BV2 2 0=0<=57V 1C2 0=3V>=52@>B8G=89 =01@O:, I> ?>2'O70=89 V7 70AB>AC20==O< V=H8E
?@5?0@0BV2, C B>@V2 \$; 20A:C;VB, 2;;NG0NG8 ?C@?C@C (5=;O9=-5=>E0.
I>:C =5@2>2>W A8AB5<8:
I>:C @5A?V@0B>@=>3> B@0:BC, >@30=V2 3@C4=>W ;;VB:8 B0 A5@54>ABV==O: :0H5;L.
I>:C B@02=>3> B@0:BC: 4V0@5O, ?0=@50B8B, 1;N20==O.
030;L=89 AB0= B0 ?>@CH5==O, ?>2O70=V 7V A?>A>I>< 70AB>AC20==O ?@5?0@0BC: =54>
<030==O.
I>:C 35?0B>1V;V0@=>W A8AB5<8: @V4:> 35?0B8B, =52V4><> ?>@CH5==O DC=:FVW ?5GV=:8.
I>:C H:V@8 B0 ?V4H:V@=>W ;;VB:>28=8: :@>?82O=:0, A25@1V6, 28A8?, D>B>GCB;82VABL,
5@8B@>45@
I>:C A:5;5B=>-<O7>2>W A8AB5<8 B0 A?>;CG=>W B:0=8=8: ;V7.
I>:C @5?@>4C:B82=>W A8AB5<8 V <>;>G=8E 70;>7: 5@5:B8;L=0 48ADC=:FVO/VB5=FVO.
I>:C =8@>: V A5G>282V4=8E H;OEV2: O: =0A;V4>: V=3V1C20==O @5=V=-0=3V>B5=78=-
0;L4>AB5@>=>2>W A8AB5<8, ?>2V4<<;O;>AO ?@> 7:, 2;;NG0NG8 =8@:>2C =54>AB0B=VABL C
?0FVT=BV2 3@C?8 @878:C; B0:V 72>W DC=:FVW <>6CBL 1CB8 >1>@>B=8<8 ?@8 ?@8?8=5==V
B5@0?VW.
A8EVG=V ?>@CH5==O: 45?@5AVO.
01>@0B>@=V ?>:07=8:8: 3V?>=0B@VT
VB8.
@>DV;L ?>1VG=8E @50:FV9 C 4VB59 ?>4V1=89 4> ?@>DV;N C 4>@>A;8E ?0FVT=BV2. 0=V
AB>A>2=> ?>1VG=8E @50:FV9 C 4VB59 >1<565=V.

5@54>7C20==O.
!8<8 V=B>:A8:0FVW. 5 ?>2V4<<;O;>AO ?@> 28?04:8 ?5@54>7C20==O ?@5?0@0BC. 09<>2V@=8<8 A8
<0<8, 70;56=> 2V4 >1 T7C20==O, 1C4CBL 0@B5@V0;L=0 3V?>B5=7VO, B0EV:0@4VO;<>6;820
1@048:0@4VO.
V:C20==O V=B>:A8:0FVW.
V:C20==O 70;568BL 2V4 B@820;>ABV G0AC, I><8=C2 ?VA;O ?@89>6 2V4 E0@0:B5@C V B06:>ABV
A8
@V>@8B5B=>N N <0T 1CB8 AB01V;V70FVO DC=:FVW A5@F52>-AC48==>W A8AB5-8. VA;O
?5@>@0;L=>3> ?@89>:070=5 70AB>AC20==O 0:B82>20=>3> 2C3V;;O C 2V4?>2V4=V9 4>7V. V7=VH5
A;V4 G0AB> :>=B@>;N20B8 >A=>2=V ?>:07=8:8 68BBT4VO;L=>ABV >@30=V7@83C20B8 ?@8
=5>1EV4=>ABV. >70@B0= B0 0:B82=V <5B01>;VB8 =5 2840;ONBLAO ?@8 ?@>2545==V 35<>4V0;V7C.

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

03VB=VABL.

V:0@AL:89 70AV1 ?@>B8?>:070=> 70AB>A>2C20B8 203VB=8< 01> 6V=:0<, O:V ?;0=CNBL
70203VB=VB8. /:I> ?V4 G0A ;V:C20==O F8< 70A>1>< ?V4B25@46CTBLAO 203VB=VABL, 9>3>
70AB>AC20==O =5>1EV4=> =5309=> ?@8?8=8B8 V 70
?V45;>3VG=V 40=V AB>A>2=> @878:C B5@0B>35==>3> 2?;82C 2=0A;V4>: 70AB>AC20==O
V=3V1VB>@V2 \$?@>BO3>< I B@8<5AB@C 203VB=>ABV =5 ?5@5:>=:82V; >4=0: =525;8:5
7@>AB0==O @878:C =5 28:;NG5=5. A:V;L:8 =5<0T :=B@>;L>20=8E 5?V45;>3VG=8E 40=8E I>4>
@878:C ?@8 70AB>AC20==V 0=B03>=VABV2 @5F5?B>@V2 0=3V>B5=78=C (), ?>4V1=V @878:8
<>6CBL VA=C20B8 V 4;O FL>3> :;0AC ?@5?0@0BV2. 0 28=OB:× 28?04:V2, :>8 ?@>4>265==O
B5@0?VW 22060TBLAO =5>1EV4=8<, ?0FVT=B:0<, O:V ?;0=CNBL 203VB=VABL, A;V4 ?@87=0G8B8
0;LB5@=0B82=C 3V?5@B5=782=C B5@0?VN 7V 2AB0=>2;5=8< ?@>DV;5< 157?5:8 I>4>
70AB>AC20==O C ?5@V>4 203VB=>ABV. /:I> 4V03=>AB>20=> 203VB=VABL, ;V:C20==O A;V4
=5309=> ?@8?8=8B8 V, O:I> =5>1EV4=>, A;V4 @>7?>G0B8 0;LB5@=0B82=5 ;V:C20==O.
V4><>, I> 70AB>AC20==O ?@>BO3>< II B0 III B@8<5AB@V2 V=4C:CT D5B>B>:A8G=VABL
(?>A;01;5==O DC=:FVW =8@>;, >;V3>3V4@0<=V>=, 70B@8A8DV:0FVW :VAB>: G5@5?0) V
=5>=0B0;L=C B>:A8G=VABL (=8@>:20 =54>AB0B=VABL, 3V?>B5=7VO, 3V?5@:0;VT
/:I> ?@>BO3>< II B@8<5AB@C 203VB=>ABV 70AB>A>2C20;8AO , @5:><5=4>20=> ?@>25AB8
C;LB@072C:>25 >1AB565==O 4;O ?5@52V@:8 DC=:FVW =8@>: V AB0=C :VAB>: G5@5?0.
!B0= =>2>=0@>465=8E, <0B5@V O:8E 70AB>A>2C20;8 , A;V4 G0AB> ?5@52V@OB8 AB>A>2=>
@>728B:C 0@B5@V0;L=>W 3V?>B5=7VW.
>4C20==O 3@C44N. A:V;L:8 =5<0T V=D>@<0FVW I>4> 70AB>AC20==O ;>70@B0=C C ?5@V>4
3>4C20==O 3@C44N, =5 @5:><5=4CTBLAO ?@87=0G0B8 F59 ?@5?0@0B. 060=5 0;LB5@=0B82=5
;V:C20==O ?@5?0@0B0<8 7 :@0I5 282G5=8< ?@>DV;5< 157?5:8 I>4> 3>4C20==O 3@C44N, >A>1;82> C
?5@V>4 =>2>=0@>465=>ABV 01> O:I> 48B8=0 =54>=>H5=0.

VB8.

57?5:0 B0 5D5:B82=VABL 70AB>AC20==O □>700@C® 4VBO< 2V:× 4> 6 @>:V2 =5 2AB0=>2;5=V.

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

V?5@GCB;82VABL

=3V>=52@>B8G=89 =01@O:. !;V4 G0AB> :=B@>;N20B8 AB0= ?0FVT=V2 7 0=3V>=52@>B8G=8<
=01@O:>< (=01@O:8 >1;8GGO, 3C1, 3>@>:0 B0/01> O78:0) 2 0=0<=57V.
@B5@V0;L=0 3V?>B5=7VO V 2>4=>-5;5:B@>;VB=89 48A10;0=A
!8<0B8G=0 0@B5@V0;L=0 3V?>B5=7VO, >A>1;82> ?VA;O 70AB>AC20==O ?5@H>W 4>78
?@5?0@0BC 01> ?VA;O ?V428I5==O 4>78 <>65 28=8:0B8 C ?0FVT=V2 7V 7=865=8<
2=CB@VH=L>AC48==8< >1T<>< 01> 45DVF8B>< =0B@VN, A?@8G8=5=8<8 70AB>AC20==O<
A8;L=8E 4VC@5B8:V2, 4VTB8G=8< >1<565==O< A?>6820==O A>;V, 4V0@5TN 01> 1;N20==O
B@51CNBL :>@5:FVW ?5@54 ?>G0B:× ;V:C20==O >700@> 7=865==O ?>G0B:>2>W 4>78 ?@5?0@0BC
(482. «!>AV1 70AB>AC20==O B0 4>78»). "0:V 6 @5:><5=40FVW AB>ACNBLAO 4VB59 2V:× 2V4 6 4>
18@>:V2.
:5:B@>;VB=89 48A10;0=A
;5:B@>;VB=89 48A10;0=A G0AB> A?>AB5@V30TBLAO C ?0FVT=V2 V7 ?>@CH5==O< DC=:FVW
=8@>: (7 01> 157 FC:@>2>3> 4V015BC), I> A;V4 1@0B8 4> C2038. # .;V=VG=>A;V465==V 70 CG0ABN
E2>@8E =0 FC:@>289 4V015B II B8?C B0 7 =5D@>?0BVTN G0AB>B0 28=8:;5==O 3V?5@:0;VTN ?@8
;V:C20==V >700@>@V2=O=> 7 ?;0F51>. "> ?5@52V@OB8 :=F5=B@0FVW :0;VN C ?;072V V ?>:07=8:8
.;V@5=AC :@50B8=V=C, >A>1;82> C ?0FVT=V2 V7 A5@F52>N =54>AB0B=VABN V .;V@5=A<
:@50B8=V=C 30-50 <;/E2.
5 @5:><5=4>20=5 >4=>G0A=5 70AB>AC20==O ?@5?0@0BC >700@® V :0;V9715@V30NG8E
4VC@5B8:V2, 4>102>: :0;VN V 70;V, I>
>@CH5==O DC=:FVW ?5GV=:8

5@CG8 4> C2038 D0@<0>:V=5B8G=V 40=V, I> 2:07CNBL =0 VAB>B=5 ?V428I5==O :>=F5=B@0FVW
>70@B0=C C ?;072V E2>@8E =0 F8@>7 ?5GV=:8, A;V4 @>73;O=CB8 ?8B0==O ?@> 7=865==O 4>78
4;O ?0FVT=BV2 V7 =0O2=VABN 2 0=0<=57V ?>@CH5=L DC=:FVW ?5GV=:8. 5<0T 4>A2V4C
70AB>AC20==O ?@5?0@0BC ?0FVT=B0< V7 BO6:8<8 ?>@CH5==O<8 DC=:FVW ?5GV=:8.
>700@® =5 @5:><5=4>20=89 4;O 70AB>AC20==O 4VBO< V7 ?>@CH5==O<8 DC=:FVW ?5GV=:8.

>@CH5==O DC=:FVW =8@>:

>2V4><;O;>AO ?@> 28=8:=5==O 7:, 2;:NG0NG8 =8@>:2C =54>AB0B=VABL, I> ?>2'07C20;8 7
?@83=VG5==O< @5=V=-0=3V>B5=78=>2>W A8AB5<8 (>A>1;82> C ?0FVT=BV2 V7 70;56=VABN
DC=:FVW =8@>: 2V4 A8AB5<8 @5=V=-0=3V>B5=78=-0;L4>AB5@>=, B>1B> ?0FVT=B8 7 BO6:8<8
?>@CH5==O<8 DC=:FVW A5@FO 01> 7 C65 VA=CNG8<8 ?>@CH5==O<8 DC=:FVW =8@>:).
@5?0@0B8, I> 2?;820NBL =0 @5=V=-0=3V>B5=78=-0;L4>AB5@>=>2C A8AB5: <>6CBL 1CB8
>1>@>B=8<8 ?VA;O ?@8?8=5==O B5@0?VW. !;V4 7 >15@56=VABN 70AB>A>2C20B8 >700@®
?0FVT=B0< V7 42>1VG=8< AB5=>7< =8@>:28E 0@B5@V9 01> 7V AB5=>7< 0@B5@VW T48=>W
=8@>:8.

0AB>AC20==O 4VBO< V7 ?>@CH5==O<8 DC=:FVW =8@>:

@5?0@0B =5 @5:><5=4>20=89 4;O 70AB>AC20==O 4VBO< 7V H284:VABN ;;C1>G:>2>W
DV;LB@0FVW

< 30 <;E/2/1,73<2, >A:V;L:8 =5<0T 2V4?>2V4=8E 40=8E I>4> 70AB>AC20==O.

@>BO3<< ?5@V>4C 70AB>AC20==O >700@C® A;V4 @53C;O@=> ?5@52V@OB8 DC=:FVN =8@>:,
>A:V;L:8 <>6;825 WW ?>3V@H0==O. A>1;82> F5 AB>ACTBLAO A8BC0FV9, :>8 ;>70@B0=
70AB>A>2CNBL ?@8 =0O2=>ABV V=H8E ?0B>;>3VG=8E AB0=V2 (30@OG:0, 453V4@0B0FVO), O:V
<>6CBL 2?;820B8 =0 =8@>:2C DC=:FVN.

4=>G0A=5 70AB>AC20==O ;>70@B0=C V V=3V1VB>@V2 \$?>3V@HCT DC=:FVN =8@>:, B>
<1V=0FVO =5 @5:><5=4>20=0.

"@0=A?:0=B0FVO =8@>:8.

5<0T 4>A2V4C I>4> 157?5:8 70AB>AC20==O ?@5?0@0BC ?0FVT=B0<, O:8< I>9=> ?@>2545=>
B@0=A?:0=B0FVN =8@>:8.

5@28==89 3V?5@0;L4>AB5@>=V7

?0FVT=BV2 V7 ?5@28==8< 3V?5@0;L4>AB5@>=V7<<<, O: ?@028;>, =5 A?>AB5@V30TBLAO 5D5:BC
?@8 70AB>AC20==V ?@5?0@0BV2, I> 4VNBL H;OE< V=3V1VFVW @5=V=-0=3V>B5=78=>2>W
A8AB5<8. ">700@® =5 @5:><5=4>20=89 4;O FVTW 3@C?8 ?0FVT=BV2.

0E2>@N20==O :>@>=0@=8E 0@B5@V9 B0 F5@51@>20A:C;O@=V 70E2>@N20==O.

/: V ?@8 70AB>AC20==V V=H8E 0=B83V?5@B5=782=8E ?@5?0@0BV2, =043> B8A:C C ?0FVT=BV2 7
VH5:0@40 01> V=AC;LBC.

15@F520 =54>AB0B=VABL.

/: V ?@8 70AB>AC20==V V=H8E ?@5?0@0BV2, I> 2?;820NBL =0 @5=V=-0=3V>B5=78=-

0;L4>AB5@>=>2C A8AB5N =54>AB0B=VABN 7/157 ?>@CH5==O DC=:FVW =8@>: VA=CT @878:

@>728B:C BO6:>W 0@B5@V0;L=>W 3V?>B5=7VW V (G0AB> 3>AB@>3>) ?>@CH5==O DC=:FVW
=8@>:.

5<0T 4>AB0B=L>3> B5@0?52B8G=>3> 4>A2V4C 70AB>AC20==O ;>70@B0=C ?0FVT=B0< V7
A5@F52>N =54>AB0B=VABN V AC?CB=V< BO6:8< ?>@CH5==O< DC=:FVW =8@>:, ?0FVT=B0< V7

BO6:>N A5@F52>N =54>AB0B=VABN (:;0A V 70 NYHA), 0 B0:>6 C ?0FVT=BV2 V7 A5@F52>N

=54>AB0B=VABN V A8<0B8G=>N =5157?5G=>N 4;O 68BBO A5@F52>N 0@8B70@B0= A;V4
70AB>A>2C20B8 7 >15@56=VABN B0:V9 3@C?V ?0FVT=BV2. !;V4 7 >15@56=VABN >4=>G0A=>

70AB>A>2C20B8 ;>70@B0= V

β-1;>:0B>@8.

!B5=>7 0>@B0;L=>3> V 3> ::0?0=V2, >1AB@C:B82=0 3V?5@B@>DVG=0 :0@4V>?0BVO.

/: V ?@8 70AB>AC20==V V=H8E 207>48;0B0B>@V2, 7 >A>1;82>N >15@56=VABN ?@87=0G0NBL

?@5?0@0B ?0FVT=B0< 7V AB5=>7< 0>@B0;L=>3> V 3> ::0?0=V2 01> >1AB@C:B82=>N

3V?5@B@>DVG=>N :0@4V>?0BVTN.

>?>28=8.

> A:;04C ?@5?0@0BC 2E>48BL ;0:B>70. 0FVT=B0< V7 B0:8<8 @V4:VA=8<8 A?04:>28<8 70E2>@N20==O
<8 O: =5?5@5=>A878, 45DVF8B><< ;0:B078 0?0 V 3;N:>7>-30;0:B>7=>N<0;L01A>@1FVTN =5 A;V4
70AB>A>2C20B8 40=89 ?@5?0@0B.

=HV 70AB5@565==O.

/: 2AB0=>2;5=> AB>A>2=> V=3V1VB>@V2 0=3V>B5=78=?5@5B2>@N20;L=>3> D5@<5=BC, ;>70@B0=
B0 V=HV 0=B03>=VAB8 0=3V>B5=78=C<5=H 5D5:B82=V C ?0FVT=BV2 G>@=>W @0A8, =V6 2
V=H8E ?0FVT=BV2, <>6;82>, G5@57 =87L:C 0:B82=VABL @5=V=C C ?0FVT=BV2 7 0@B5@V0;L=>N
3V?5@B5=7VTN, O:V T ?@54AB02=8:0<8 G>@=>W @0A8.

**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.**

5 ?@>2>48;8AO 4>A;V465==O I>4> 2?;82C ?@5?0@0BC =0 740B=VABL C?@02;OB8 02B>B@0=A?>@B>
<V <5E0=V7<0<8. 4=0: A;V4 ?0<OB0B8 ?@> <>6;82VABL @>728B:C B0:8E ?>1VG=8E @50:FV9 O: 70?0
<>@>G5==O B0 A>=;82VABL, >A>1;82> =0 ?>G0B:C ;V:C20==O B0 ?@8 ?V428I5==V 4>78 ?@5?0@0BC.

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

=HV 3V?>B5=782=V ?@5?0@0B8 <>6CBL ?>A8;N20B8 3V?>B5=782=89 5D5:B ;>70@B0=C. 4=>G0A=5
70AB>AC20==O 7 V=H8<8 ?@5?0@0B0<8, I> <>6CBL V=4C:C20B8 B0:C ?>1VG=C @50:FVN O:
0@B5@V0;L=0 3V?>B5=7VO (B@8F8;:VG=V 0=B845?@5A0=B8, 0=B8?A8E>B8G=V 70A>18, 10;:>D5=
V 0AB8=), <>65 ?V428IC20B8 @878: 28=8:=5==O 0@B5@V0;L=>W 3V?>B5=7VW.

>70@B0= <5B01>;V7CTBLAO ?5@5206=> 70 CG0ABN A8AB5<8 F8B>E@>CYP) 219 4> 0:B82=>3>
:0@1>:A8=:8A;>3> <5B01>;VBC. # :;V=VG=8E 4>A;V465==OE 1C;> 2AB0=>2;5=>, I> D;C:>=07>;
(V=3V1VB>@ CYP2!9) 7=86CT 5:A?>78FVN 0:B82=>3> <5B01>;VBC ?@81;87=> =0 50%. AB0=>2;5=>,
I> >4=>G0A=5 ;V:C20==O ;>70@B0=<< V @8D0< (V=4C:B>@ D5@<5=BV2 <5B01>;V748BL 4>
7=865==O =0 40 % :>=F5=B@0FVW 0:B82=>3> <5B01>;VBC C ?;072V. ;V=VG=5 7=0G5==O FL>3>
5D5:BC =52V4><5. 5<0T 2V4ABV 2 5:A?>78FVW ?@8 >4=>G0A=>AC20==V ;>70@B0=C V
D;C20AB0B8=C (A;01:>3> V=3V1VB>@C CYP2!9).

"0: A0<>, O: V ?@8 70AB>AC20==V V=H8E ?@5?0@0BV2, O:V 1;:>CNBL 0=3V>B5=78= II 01> 9>3>
5D5:B8, AC?CB=T 70AB>AC20==O ?@5?0@0BV2, I> 70B@8@30=V7=>;0:B>=C, B@V0@84C), 01>
<>6CBL ?V428IC20B8 @V2=V :0;VN (=0?@8;:04, 35?0@8=), 4>40B:V2, I> 70;V, I>20BFV :@>2V.
4=>G0A=5 70AB>AC20==O B0:8E 70A>1V2 =5 @5:><5=4>20=5.

@> >1>@>B=5 ?V428I5==O :>=F5=B@0FV9 ;VBN C A8@>20BFV :@>2V, 0 B0:>6 ?@> B>:A8G=VABL
?>2V4><;O;>AO ?@8 >4=>G0A=>AC20==V ;VBN 7 V=3V1VB>@0<8 \$. "0:>6 4C65 @V4:> ?>2V4>
<;O;>AO ?@> 28?04:8 ?@8 70AB>AC20==V 0=B03>=VABV2 @5F5?B>@V2 0=3V>B5=78=C. 4=>G0A=5
;V:C20==O ;VBN V ;>70@B0=C A;V4 ?@>2>48B8 7 >15@56=VABN. /:I> 70AB>AC20==O B0:>W :>
<1V=0FVW 22060TBLAO =5>1EV4=8<, @5:><5=4>20=> ?5@52V@OB8 @V2=V ;VBN C A8@>20BFV
:@>2V ?@>B03>< :><1V=>20=>3> ;V:C20==O.

@8 >4=>G0A=>AC20==V 0=B03>=VABV2 0=3V>B5=78=C V =5AB5@>W4=8E ?@>B870?0;L=8E
?@5?0@0BV2 (=0?@8;:04, A5;5:B82=V V=3V1VB>@8 F8;:>:A835=078-2 (&-2), 0F5B8;A0;VF8;>20
:8A;>B0 C 4>70E, I> G8=OBL ?@>B870?0;L=C 4VN, =5A5;5:B82=V) <>65 ?>A;01;N20B8AO
0=B83V?5@B5=782=89 5D5:B. 4=>G0A=5 70AB>AC20==O 0=B03>=VABV2 0=3V>B5=78=C 01>
4VC@5B8:V2 V7 <>65 ?@872>48B8 4> ?V428I5==O @878:C ?>3V@H0==O DC=:FVW =8@>;,
2;:NG0NG8 <>6;8289 @>728B>: 3>AB@>W =8@:>2>W =54>AB0B=>ABV, 0 B0:>6 4> ?V428I5==O
@V2=O :0;VN C A8@>20BFV :@>2V, >A>1;82> C ?0FVT=BV2 7 VA=CNG& ?>@CH5==O< DC:FVW
=8@>:. "0:C :><1V=0FVN A;V4 ?@87=0G0B8 7 >15@56=VABN, >A>1;82> ?0FVT=B0< ;VB=L>3> 2V:C.
0FVT=B0< A;V4 ?@>2>48B8 2V4?>2V4=C 453V4@0B0FVN, B0:>6 A;V4 @>73;O=CB8 ?8B0==O I>4>
<=>VB>@8=3C DC=:FVW =8@>: ?VA;O ?>G0B:C AC?CB=L>W B5@0?VW, =040;V ?5@V>48G=>.

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

\$0@<0:>48=0

>70@B0= F5 A8=B5B8G=89 0=B03>=VAB @5F5?B>@V2 0=3V>B5=78=C (B8?C ") 4;O ?5@>@0;L=>3>
70AB>AC20==O. =3V>B5=78= II ?>BC6=89 207>:>=AB@8:B>@ T 0:B82=8< 3>@<=>< @5=V=
0=3V>B5=78=>2>W A8AB5<8 V >4=8< 7 =09206;82VH8E D0:B>@V2 ?0B>DV7V>;>3VW
0@B5@V0;L=>W 3V?5@B5=7VW. =3V>B5=78=II 72'O7CTBLAO 7 @5F5?B>@>< "1, O:89 7=0945=> C
1030BL>E B:0=8=0E (=0?@8;:04, C 3;04:8E <O70E AC48=, =04=8@:>28E 70;>70E, =8@:0E V A5@FV),
287=0G0NG8 =87:C 206;828E 1V>;>3VG=8E 5D5:BV2, C B>:>=AB@8:FVN V 72V;L=5==O
0;L4>AB5@>=C. =3V>B5=78= II B0:>6 AB8;VD5@0FVN 3;04:><'O7>28E ;:VB8=.

>70@B0= A5;5:B82=> 72'O7CTBLAO 7 @5F5?B>@<> "1. C<>20E V? vitro B0 V? vivo ;>70@B0= B0 9>3> D0@<0:>;>3VG=> 0:B82=89 <5B01>;VB :0@1>:A8;L=0 :8A;>B0 (-3174) 1;>:CNBL CAV DV7V>;>3VG=> 203>B5=78=C II, =570;56=> 2V4 465@5;0 01> H;OEC A8=B57C.

>70@B0= A5;5:B82=> 72'O7CTBLAO 7 @5F5?B>@<> "1, =5 72'O7CTBLAO V =5 1;>:CT V=HV @5F5?B>@8 3>@<>=V2 01> V>=V :0=0;8. V;LH5 B>3>, ;>70@B0= =5 ?@83=VGCT \$ (:V=V=07CII) D5@<5=B, O:89 A?@8OT @>7?04C 1@048:V=V=C. #=0A;V4>: FL>3> 5D5:B8, 157?>A5@54=L=> =5 ?>2'O70=V 7 1;>:04>N @5F5?B>@0 "1, B0:V O: ?>A8;5==O 2?;82V2, <54V0B>@<> O:8E T 1@048:V=V=, =5 0A>FV9>20=V V7 70AB>AC20==O< ;>70@B0=C.

V4 G0A 70AB>AC20==O ;>70@B0=C CAC=5==O =530B82=>W >1>@>B=>W @50:FVW 0=3V>B5=78=C =0 A5:@5FVN @5=V=C ?@872>48BL 4> ?V42815==O 0:B82=>ABV @5=V=C C ?;072V. "0:5 ?V42815==O 0:B82=>ABV ?@872>48BL 4> 7@>AB0==O 0=3V>B5=78=C C ?;072V. %>G0 2V41C20TBLAO B0:5 7@>AB0==O, 0=B83V?5@B5=782=0 0:B82=VABL V AC?@5AVO :=F5=B@0FVW 0;L4>AB5@>=C C ?;072V 715@V30NBLAO, I> A2V4G8BL ?@> 5D5:B82=C 1;>:04C @5F5?B>@V2 0=3V>B5=78=C . VA;O 2V470@B0=C 0:B82=VABL @5=V=C C ?;072V V ?>:07=8:8 @V2=V2 0=3V>B5=78=C ?@>BO3< 3 4=V2 ?>25@B0NBLAO 4> ?>G0B:>28E 7=0G5=L.

/: ;>70@B0=, B0: V 9>3> >A=>2=89 <5B01>;VB <0NBL 28IC A?>@V4=5=VABL 4> "1 @5F5?B>@V2, =V6 "2. :B82=89 <5B01>;VB C 10-40 @07V2 0:B82=VH89, =V6 ;>70@B0=.

0AB>AC20==O ;>70@B0=C 40T 7<>3C 7<5=H8B8 7030;L=C :V;L:VABL ;5B0;L=8E 28?04:V2 V7 A5@F52>-AC48==8E ?@8G8=, V=AC;LBC B0 V=D0@:BC :0@40 C E2>@8E =0 0@B5@V0;L=C 3V?5@B5=7VN 7 3V?5@B>DVTN ;V2>3> H;C=>G:0, 70157?5GCT 70E8AB =8@>: C E2>@8E =0 FC:@>289 4V015B II B8?C 7 ?@>B5W=C@VTN.

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

IA>@IFVO

VA;O ?5@>@0;L=>3> ?@89>70@B0= 4>1@5 2A<>:BCTBLAO V ?V4;O30T <5B01>;V73> ?@>E>465==O 7 D>@ 33 %. !5@54=V ?V:>2V :=F5=B@0FVW ;>70@B0=C B0 9>3> 0:B82=>3> <5B01>;VBC 4>AO30NBLAO 2V4?>2V4=> G5@57

1 3>48=C V 3-4 3>48=8.

>7?>4V;

>70@B0= V 9>3> 0:B82=89 <5B01>;VB =0 □ 99 % 72'O7CNBLAO 7 ?@>B5W=0<8 ?;07<8 :@>2V, ?5@54CAV< 7 0;L1C

V>B@0=AD>@<0FVO

@81;87=> 14 % ;>70@B0=C ?@8 2=CB@VH=L>25==> ?5@>@0;L=>AC20==V ?5@5B2>@NTBLAO =0 0:B82=89 <5B01>;VB. VA;O 2=CB@VH=L>25==>3> V ?5@>@0;L=>3> 22545==O ;>70@B0=C :0;VN,3> 14!, @04V>0:B82=VABL C F8@:C;NNGV9 ?;072V, O: ?@028;>, E0@0:B5@87CTBLAO ;>70@B0=< B0 9>3> <5B01>;VB>

82545==O

;07<>289 :;V@5=A ;>70@B0=C B0 9>3> 0:B82=>3> <5B01>;VBC AB0=>28BL 600 <;/E2 V 50 <;/E2 2V4?>2V4=>. 8@>:289 :;V@5=A ;>70@B0=C B0 9>3> 0:B82=>3> <5B01>;VBC AB0=>28BL ?@81;87=>

74 <;/E2 V 26 <;/E2 2V4?>2V4=>. >;8 ;>70@B0= 70AB>A>2CNBL ?5@>@0;L=>, ?@81;87=> 4 % 4>78 284V;OTBLAO C =57 6 % 4>78 284V;OTBLAO V7 A5G5N C 283;O4V 0:B82=>3><5B01>;VBC. \$0@ <0:>:V=5B8G=V 2;0AB82>ABV ;>70@B0=C B0 9>3> 0:B82=>3> <5B01>;VBC ;V=V9=V ?@8 ?5@>@0;L=8E 4>70E ;>70@B0=C :0;VN 4> 200 <3.

VA;O ?5@>@0;L=>3> 70AB>AC20==O :=F5=B@0FVW C ?;072V ;>70@B0=C B0 9>3> 0:B82=>3> <5B01>;VBC 7<5=HCNBLAO ?>;V5:A?>=5=FV9=> 7 B5@ G0A<< =0?V2282545==O ?@81;87=> 2 3>48=8 V 6-9 3>48= 2V4?>2V4=>. VA;O ?5@>@0;L=>3> ?@89>14!<0@>:20=>3> ;>70@B0=C ?@81;87=> 35 % @04V>0:B82=>ABV 7=0E>4OBL C A5GV, 058 % C :0;V.

\$0@<0:>:V=5B8:0 2 >:@5<8E 3@C?0E ?0FVT=BV2

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

>=F5=B@0FVW ;>70@B0=C B0 9>3> 0:B82=>3> <5B01>;VBC C ?;072V ?0FVT=BV2 ;VB=L>3> 2V:C 7 0@B5@V0;L=>N 3V?5@B5=7VTN 7=0GCI=>=5 @V7=OBLAO 2V4 40=8E ?>:07=8:V2 C <>;>48E ?0FVT=BV2 7 0@B5@V0;L=>N 3V?5@B5=7VTN.

!B0BL

>=F5=B@0FVW ;>70@B0=C C ?;072V 1C;8 C 2 @078 28IV C 6V=>: 7 0@B5@V0;L=>N 3V?5@B5=7VTN
?>@V2=O=> 7 G>;>2V:0<8. >=F5=B@0FVW 0:B82=>3> <5B01>;VBC C G>;>2V:V2 V 6V=>: =5
@V7=8;8AO.

>@CH5==O DC=:FVW ?5GV=:8 B0 =8@>:

@8 ?@89> ?0FVT=B0<8 7 ;53:8< B0 ?>2V 28O2;O;8AO 2V4?>2V4=> C 1,7- 5 @078 1V;LH5, =V6 C
<>;>48E 4>1@>2>;LFV2 G>;>2VG>W AB0BV.

>=F5=B@0FVW ;>70@B0=C C ;072V C ?0FVT=V2 V7 ;:V@5=A<< :@50B8=V=C 28I5 10 <;E2 =5
2V4@V7=O;8AO 2V4 B0:8E 2 >AV1 V7 =57N DC=:FVTN =8@>:. @8 ?>@V2=O==V ?;>IV ?V4 :@82>N
:>=F5=B@0FVW () C ?0FVT=V2 V7 =>@<0;L=>N =8@>:2>N DC=:FVTN ;>70@B0=C C E2>@8E, O:V
?5@51C20NBL =0 3><>B@0=A?;0=B0FVW, 28O28;0AO ?@81;87=> C 2 @078 1V;LH>N. ;07<>2V
:>=F5=B@0FVW 0:B82=>3> <5B01>;VBC =5 7@CH5==O< DC=:FVW =8@>: 01> E2>@8E, O:V
?5@51C20NBL =0 35<>4V0;V7V.>70@B0= V 9>3> 0:B82=89 <5B01>;VB =5 <>6CBL 1CB8 28;CG5=V 70
4>?><>3>N 35<>4V0;V7C.

\$0@<0>:V=5B8:0 C 4VB59.

\$0@<0>:V=5B8:0 ;>70@B0=C 282G0;0AO 70 CG0ABN 50 4VB59 7 0@B5@V0;L=>N 3V?5@B5=7VTN,
2V:<< 2V4 1 16 @>:V2, ?VA;O ?5@>@0;L=>3> 70AB>AC20==O 1 @07 =0 4>1C C 4>70E 2V4 0,54 4> 0,77
<3/:3 (A5@54=V 4>78). 57C;LB0B8 ?>:070;8, I> 0:B82=89 <5B01>;VB ;>70@B0=C CB2>@NTBLAO C
?0FVT=V2 CAVE 2V:>28E 3@C?. 57C;LB0B8 2:07CNBL =0 ?@81;87=> 0=0;>3VG=V ?>:07=8:8 D0@
<0>:V=5B8:8 ;>70@B0=C ?VA;O ?5@>@0;L=>3> 70AB>AC20==O C =>2>=0@>465=8E V 4VB59 2V:<<
4> 2 @>:V2, 4VB59 4>H:V;L=>3>, H:V;L=>3> 2V:C V C ?V4;VB:V2. \$0@<0>:V=5B8G=V ?>:07=8:8
<5B01>;VBC 2V4@V7=O;8AO 1V;LH5 70;56=> 2V4 2V:>2>W 3@C?8. @8 ?>@V2=O==V 4VB59
4>H:V;L=>3> 2V:C V ?V4;VB:V2, B0:V 2V4ABV 1C;8 AB0B8AB8G=> 7=0GCI8<8. :A?>78FVO C
=>2>=0@>465=8E V 4VB59 4> 2 @>:V2 1C;0 ?>@V2=O=> 28A>:N.

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

A=>2=V DV78:>-EVABV:

4;O 4>7C20==O 50 <3: >20;L=V B01;5B:8, 2:@8BV ?;V2:>2>N >1>;>=:>N, 1V;>3> :>;L>@C, 7
3@02V@C20==O< «952» 7 >4=>3> 1>:C B0 =0AVG:>N 7 V=H>3>;
4;O 4>7C20==O 100 <3: B01;5B:8 :0?;5?>4V1=>W D>@<8, 2:@8BV ?;V2:>2>N >1>;>=:>N 1V;>3>
:>;L>@C, 7 3@02V@C20==O< «960» 7 >4=>3> 1>:C B0 3;045=L:V 7 V=H>3>.

"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 ?@8 B5@83V=0;L=V9 C?0:>2FV. 15@V30B8 C =54>ABC?=>

#?0:>2:0. > 14 B01;5B>: C 1;VAB5@V. > 2 1;VAB5@8 C :0@B>==V9 :>@>1FV.

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

8@>1=8:.

5@: (0@? V >C< V1@8B0=VO.

5@: (0@? V >C< ..., V45@;0=48/

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VAF57=0E>465==O.

(>BB=> 59=, @0<;V=3B>=, >@BC<15@;5=4 NE23 3JU, 5;8:>1@8B0=VO.

00@45@253 39, 2031 %00@;5<, V45@;0=48/

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