

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

"
(METOPROLOL)

!,:04:
4VNG0 @5G>28=0: <5B>?@>;;
1 B01;5B:0 C ?5@5@0EC20==V =0 100 % @5G>28=C 25 <3 01> 50 <3, 01> 100 <3;
4>?>28=8: ;0:B>70, <=>3V4@0B; F5;N;>70 :@8AB0;VG=0; :@>A?>2V4>=; ?>2V4>=; B0;L;; :0;LFDVN
AB50@0B.

V:0@AL:0 D>@<0. "01;5B:8.
A=>2=V DV78:>-EVABV: B01;5B:8 :@C3;>W D>@<8 7 ?>A:>N ?>25@E=5N, 1V;>3> 01> 1V;>3> 7 :@5

\$0@<0:>B5@0?52B8G=0 3@C?0. !5;5:B82=V 1;>:0B>@8 □-04@5=>@5F5?B>@V2.
>4 "% !0702.

\$0@<0:>;>3VG=V 2;0AB82>ABV.
\$0@<0:>48=0
5B>?@>;; □₁-A5;5:B82=89 1;>:0B>@ 04@5=5@3VG=8E @5F5?B>@V2 157 2=CB@VH=L>W A8□₁-
@5F5?B>@V2. <5=HCT ?>B@51C :0@40 C :8A=V ?@8 =020=B065==V, I><0T ?>78B82=C 4VN ?@8
B@820;>:0@4VW (7<5=H5==O G0AB>B8 1>;L>28E =0?04V2). =86CT A8AB>;VG=89 0@B5@V0;L=89
B8A:;>A>1;82> ?VA;O =0?@C65==O, V 70?>1V30T @>728B:C @5D;5:B>@=>W >@B>AB0B8G=>W
3V?>B5=7VW. =865==O 4V0AB>;VG=>3> 0@B5@V0;L=>3> B8A:C =0AB0T G5@57 :V;L:0 B86=V2
@53C;O@=>3> 70AB>AC20==O. 5B>?@>;; 7=86CT ?;07<0B8G=C 0:B82=VABL @5=V=C.
\$0@<0:>:V=5B8:0.
A<>:BC20==O B0 @>?>4V; VA;O ?5@>@0;L=>3> 70AB>AC20==O <5B>?@>;; ?>2=VABN
01A>@1CTBLAO. >=F5=B@0FVO <5B>?@>;;C C ?;072V ;V=V9=> 70;568BL 2V4 268B>W 4>78 C
<560E B5@0?52B8G=8E 4>7. 0:A8<0;L=0 :=F5=B@0FVO C ?;072V (!_{max}) 4>AO30TBLAO ?@81;87=>
G5@57 1,5-2 3>48=8 ?VA;O 70AB>AC20==O (T_{max}). %>G0 :=F5=B@0FVO C ?;072V T @V7=>N C
@V7=8E >AV1, V=482V4C0;L=0 2V4B2>@N20=VABL T E>@>H>N. # @57C;LB0BV 206;82>3> ?5@H>3>
5D5:BC ?V4 G0A ?@>E>465==O G5@57 ?5GV=:C A8AB5<=0 1V>;>3VG=0 4>ABC?=VABL <5B>?@>;;C
?VA;O 70AB>AC20==O >4=VTW >@0;L=>W 4>78 4>AO30T ?@81;87=> 50 %. VA;O ?>2B>@=>3>
70AB>AC20==O 2>=0 71V;LHCTBLAO 4> 70 %. 0AB>AC20==O ?V4 G0A W6V <>65 71V;LH8B8
1V>;>3VG=C 4>ABC?=VABL =0 30-40 %. >:07=8: A?>;CG5==O <5B>?@>;;C 7 ?@>B5W=0<8 ?;07<8 T
=86G8< (?@81;87=> 5-10 %).
5B01>;V7< V 282545==O 7 >@30=V7 5B>?@>;; <5B01>;V7CTBLAO C ?5GV=FV, ?@8 FL>@NNBLAO
B@8 <5B01>;VB8, O:V =5 <0NBL ;V=VG=> 7=0GCI>3> β-1;>;CNG>3> 5D5:BC.
0728G09 1V;LH5 95 % ?5@>@0;L=>W 4>78 ?@5?0@0BC 282>48BLAO V7 A5G5N. @81;87=> 5 % 40=>W
4>78 282>48BLAO V7 A5G5N C =57:@5<8E 28?04:0E :V;L:VABL ?@5?0@0BC, I> 282>48BLAO V7
A5G5N C =57
?0FVT=BV2 ;VB=L>3> 2V:C =5 A?>AB5@V30TBLAO 7=0G=8E 7
!8AB5<=0 1V>4>ABC?=VABL B0 282545==O <5B>?@>;;C =5 72>N =54>AB0B=VABN. ;5 282545==O
<5B01>;VBV2 C B0:8E ?0FVT=BV2 7<5=H5=5. # E2>@8E 7V H284:VABN ;C1>G:>2>W DV;LB@0FVW
<5=H5 5 <;E2 2V41C20TBLAO 7=0G=5 =0:>?8G5==O <5B01>;VBV2. "0:5 =0:>?8G5==O <5B01>;VBV2
=5 <0T β-1;>;CNG>3> 5D5:BC.
?0FVT=BV2 7V 7=865=>N DC=:FVTN ?5GV=:8 D0@<0:>:V=5B8:0 <5B>?@>;;C (C 7207:C 7 =87L:8<
@V2=5< 7207C20==O 7 1V;;<8) 7N N. 4=0: C ?0FVT=BV2 7 F8@>7>< ?5GV=:8 1V>4>ABC?=VABL
<5B>?@>;;C <>65 71V;LHC20B8AO, 0 7030;L=89 ;V@5=A 7<5=HC20B8AO.

;V=VG=V E0@0:B5@8AB8:8.
>:070==O.
- @B5@V0;L=0 3V?5@B5=7VO.
- !B5=>:0@4VO (C B>ABV=D0@:B=0).

- □@8B
->?5@5465==O A5@F52>W A<5@BV B0 ?>2B>@=>3> V=D0@:BC ?VA;O 3>AB@>W D078 V=D0@:BC :0@40.
- # A:;04V :>W B5@0?VW ?@8 B8@5>B>:A8:>7V.
- @>DV;0:B8:0=0?04V2

@>B8?>:070==O.

- V428I5=0 GCB;82VABL 4> 1C4L-O:>3> :>5=B0 ?@5?0@0BC 01> 4> V=H8E β-1;>:0B>@V2;
- 0B@V>25=B@8:C;O@=0 1;>:040 (II V III ABC?5=V2), A8=>0B@V0;L=0 1;>:040;
- A8=4@>< A;01:>ABV A8=CA>2>3> 2C7;0;
- 45:>20=0 A5@F520 =54>AB0B=VABL (=01@O: ;535=V2, A8=4@>× 3V?>?5@DC7VW 01> 0@B5@V0;L=>W 3V?>B5=7VW);
- 28@065=0 1@048:0@4VO (!! ≤ 50 70 1 E2);
- :0@4V>35==89 H>;;
- BO6:V ?>@CH5==O ?5@8D5@8G=>3> :@>2>>1V3C 7 1>;5< 01> B@>DVG=8<8 7
- 0@B5@V0;L=0 3V?>B5=7VO (A8AB>;VG=89 0@B5@V0;L=89 B8A: < 100 << @B.AB.);
- 1@>=EV0;L=0 0AB<0, BO6:0 D>@<0 E@>=VG=8E >1AB@C:B82=8E 1@>=E>;535=528E 70E2>@N20=L;
- <5B01>;VG=89 0F84>7;
- =5;V:>20=0 D5>E@><>F8B><0;
- B@820;0 01> ?5@V>48G=0 V=>B@>?=0 B5@0?VO 03>=VAB0<8 β-@5F5?B>@V2;
- AC?CB=O B5@0?VO V=3V1VB>@0<8 <=>0>:A84078-□;
- 70AB>AC20==O <5B>?@>;>;C ?@>B8?>:070=> E2>@8<, O:8< ?@>2>48BLAO 2=CB@VH=L>25==5 22545==O 0=B03>=VABV2 :0;LFVN B8?C 25@0?0 V=H8E 0=B80@8B?V@0 5B>?@>;>; =5 A;V4 ?@87=0G0B8 ?0FVT=B0< 7 ?V4>7@>N =0 3>AB@89 V=D0@:B :0@40 ?@8 G0AB>BV A5@F528E A:>@>G5=L<5=H5 50 C4/E2, V=B5@20;>< P Q>0,24 c 01> A8AB>;VG=8< 0@B5@V0;L=8< B8A:>< <100 << @B.AB.
0FVT=B0< 7 45:>20=>N A5@F52>N =54>AB0B=VABN, O:V 4>1@5 ?5@5=>AOBL V=HV ;V:0@AL:V 70A>18, 70AB>AC20==O <5B>?@>;>;C <>6;825 ?@8 V=482V4C0;L=>@V 4>78.

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

0FVT=B8 ?>28==V 7=0E>48B8AO ?V4 @5B5;L=8< =03;O4><, O:I> 2>=8 >4=>G0A=> 7 ?@5?0@0B>< 5B>?@>;>; ?@89<0NBL 30=3;V>1;>:0B>@8, V=HV β-1;>:0B>@8 (=0?@8:;04, >G=V :@0?;V) 01> V=3V1VB>@8 <=>0>:A84078 (V-).
4=>G0A=>3> ?@87=0G5==O 7 ?@>?0D5=>=>< A;V4 C=8:0B8. @>?0D5=>= ?@83=VGCT <5B01>;V7< <5B>?@>;>;C G5@57 F8B>E@>< 450 2D6. 57C;LB0B B0:>W :><1V=0FVW =5?5@5410GC20=89, >A:V;L:8 ?@>?0D5=>= B0:>6 <0T β-1;>;CNGV 2;0AB82>ABV.
@8 @0?B>2V9 2V4=V48=C =0 B;V ;V:C20==O β-1;>:0B>@0<8 <>65 ?V428I8B8AO 0@B5@V0;L=89 B8A.: /:I> =5>1EV4=> 2V4=V48=><, β-1;>:0B>@ 20@B> 2V4 2V4=V48=C.
?0FVT=BV2, O:V >4=>G0A=> 7 ?@5?0@0B>< 5B>?@>;>; ?@89<0NBL 0=B03>=VAB8 :0;LFVN 25@0?0 2>3> B8?C 01> 48;BV075< B0/01> ?@5?0@0B8 4;O ;V:C20==O 0@8B7C 7C?8=:8 A5@FO). β-1;>:0B>@8 <>6CBL ?V4A8;N20B8 =530B82=V V=>B@>?=V B0 E@>=>B@>?=V 5D5:B8 ?@5?0@0BV2 4;O ;V:C20==O 0@8B38 EV=V48=C 01> 040@>=). 70T<>4VO 7 040@>=>< (28@065=0 A8=CA>20 1@048:0@4VO) <>65 28=8:0B8 ?@>BO3>< B@820;>3> G0AC ?VA;O 2V4> ?@5?0@0BC.
?0FVT=BV2, O:V >45@6CNBL ;V:C20==O β-1;>:0B>@0<8, V=30;OFV9=V 0=5AB5B8:8 ?V4A8;NNBL :0@4V>45?@5A82=89 5D5:B. =4C:B>@8 01> V=3V1VB>@8 <5B01>;V72V. >=F5=B@0FVO <5B>?@>;>;C C ?;07
@8 AC?CB=L<5B0F8=>< 01> V=H8<8 ?@5?0@0B0<8, I> ?@83=VGCNBL ?@>AB03;0=48=-A8=B5B07C, 0=B83V?5@B5=782=89 5D5:B β-1;>:0B>@V2 <>65 7<5=HC20B8AO.
0@4V>A5;5:B82=V β-1;>:0B>@8 7=0G=> <5=H>N N ?;820NBL =0 0@B5@V0;L=89 B8A: ?@8 22545==V ?0FVT=B0< 04@5=0;V=C, =V6 =5A5;5:B82=V β-1;>:0B>@8.
8;BV075< B0 1;>:0B>@8 β-@5F5?B>@V2 <0NBL 048B82=C V=3V1CNGC 4VN =0 AV-?@>2V4=VABL B0 DC=:FVN A8=CA>2>3> 2C7;0. @8 FL>

;:>0B>@8 β-@5F5?B>@V2 <>6CBL ?@>2>:C20B8 ?0@04>:A0;L=V 3V?5@B5=782=V @50:FVW C
?0FVT=BV2, O:V 70AB>A>2CNBL 28A>:V 4>78 D5=V;?@>?0=>;0
@8 AC?CB=L>:0B>@V2 7 V=AC;V=>< 01> ?5@>@0;L=8<8 0=B84V015B8G=8<8 70A>10<8 <>65
?>A8;N20B8AO 01> ?@>;>=3C20B8AO WE=O 4VO. @8 FL>A>1;82> B0EV:0@4VO V B@5<>@) <>6CBL
<0A:C20B8AL 01> 7=8:0B8. # B0:8E 28?04:0E =5>1EV4=> ?@>2>48B8 @53C;O@=89 :>=B@>;L @V2=O
3;N:>78 2 :@>2V.
!;V4 C=8:0B8 >4=>G0A=>3> ?@89>2V <>6CBL 2?;820B8 ?@5?0@0B8, I> V=3V1CNBL CYP 2D6,
=0?@8::04, EV=V48=, B5@1V=0DV=, ?0@>:A5B8=, D;C>:A5B8=, A5@B@0;V=, F5;5>:A81,
?@>?0D5=>= B0 48D5=3V4@0G0B:C ;V:C20==O F8<8 ?@5?0@0B0<8 <>65 28=8:=CB8 =5>1EV4=VABL 7
<5=H5==O 4>78 <5B>?@>;>;C.
4=>G0A=5 70AB>AC20==O 3;V:>784V2 =0?5@ABO=:8 V 1;>:0B>@V2 β-@5F5?B>@V2 <>65
71V;LHC20B8 G0A AV-?@>2V4=>ABV B0 A?@8G8=8B8 1@048:0@4VN. 8D5=3V4@0CYP 2D6 2 >AV1,
O:V <0NBL H284:C 3V4@>:A8;OFVN. D5:B8 <5B@>?@>;>;C ?>A8;NNBLAO. >6;82>, 48D5=3V4@0CYP
2D6.
8D065 AB82V.
!;V4 4>B@815@56=>ABV ?@8 :><1V=0FVW 7 =VB@0B0<8 G5@57 @878: 0@B5@V0;L=>W
3V?>B5=7VW B0/01> 1@048:0@4VW.

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

@8 ?@89>β-1;>:0B>@V2, =5>1EV4=> :>=B@>;N20B8 G0AB>BC A5@F528E A:>@>G5=L (!!) B0
0@B5@V0;L=89 B8A: (") (A?>G0B:C I>4=O, ?>BV< 1 @07 =0
0FVT=B0<, O:V ?@89<0NBL β-1;>:0B>@8, =5 A;V4 22>48B8 2=CB@VH=L>25==> 0=B03>=VAB8
:0;LFVN 25@0?02>3> B8?C.
?0FVT=BV2, O:V >B@8:0B>@8, 04@5=0;V= <>65 ?V428I8B8 0@B5@V0;L=89 B8A: V A?@8G8=8B8
(@5D;5:B>@=C) 1@048:0@4VN; FO @50:FVO <5=H V<>2V@=0 ?@8 70AB>AC20==V A5;5:B82=8E β-
1;>:0B>@V2.
5B>?@>;>; <>65 ?>A8;8B8 VA=CNGC 1@048:0@4VN.
A:V;L:8 ?5@54 EV@C@3VG=>N>?5@0FVTN <5B>?@>;>; =5>1EV4=> 2V448= 4> >?5@0FVW, 70
28=OB:><>A>1;828E 28?04:V2, =0?@8::04 B8@5>B>:A8:>7C 01> D5>E@><>F8B><8.
4=0: C 45O:8E 28?04:0E 22545==O β-1;>:0B>@V2 ?5@54 >?5@0FVTN <>65 1CB8 :>@8A=8<, >A:V;L:8
2>=8 <>6CBL 7=86C20B8 0@8B<>35==V 5D5:B8 V 7<5=HC20B8 :>@>=0@=89 :@>2>>1V3 ?@8
EV@C@3VG=> A?@8G8=OT ?5@5203C A8> B>=CAC. /:I> V7 F8E A>2C20B8 β-1;>:0B>@, A;V4
281@0B8 0=5AB5B8: 7V A;01:>N =530B82=>N V7>B@>?=>N 4VTN, I>1 7<5=H8B8 @878:
?@83=VG5==O :0@40.
> ?@>2545==O 7030;L=>W 0=5AB57VW ;V:0@-0=5AB57V>;>3 ?>28=5= 1CB8 ?>V=D>@<>20=89 ?@>
B>9 D0:B, I> ?0FVT=B 70AB>A>2CT 5B>?@>;>;. 5 @5:>5=4CTBLAO ?@8?8=OB8 ;V:C20==O ?V4 G0A
?@>2545==O EV@C@3VG=>3> 2B@CG0==O.
C65 @V4:> <>6CBL ?>A8;8B8AO @0=VH5 VA=CNGV ?>@CH5==O ?5@54A5@4=>-H;C=>G:>2>W
?@>2V4=>ABV, V=>4V 7 @>728B:< ?5@54A5@4=>-H;C=>G:>2>W 1;>:048.
V>4>ABC?=VABL <5B>?@>;>;C <>65 ?V428IC20B8AO ?@8 F8@>7V ?5GV=:8.
/: ?@028>;, ?@8 ;V:C20==V E2>@8E =0 0AB C O:>ABV AC?CB=L>W B5@0?VW A;V4 ?@87=0G0B8
β₂-03>=VAB8 (C B01;5B:0E 01> 05@>7>;V). # 28?04:0E :>;8FV ?0FVT=B8 ?>G8=0NBL ?@89<0B8
?@5?0@0B, <>65 7=04>18B8AO 71V;LH5==O 4>78 β₂-03>=VABV2. 878:, I>?@5?0@0B 1C45 2?;820B8 =0
β₂-@5F5?B>@8, =86G89, =V6 C 28?04:C 70AB>AC20==O 728G09=8E =5A5;5:B82=8E β₁-1;>:0B>@V2 C
B01;5B:0E.
A>1;82> @5B5;L=89 ;V:0@AL:89 :>=B@>;L =5>1EV4=89 ?@8 ;V:C20==V E2>@8E =0 FC:@>289 4V015B
(:>=B@>;L @V2=O 3;N:>78 2 :@>2V), ?0FVT=BV2 7 =5AB01V;L=8< @V2=5< FC:@C 2 :@>2V, ?@8
70AB>AC20==V AC2>@>W 4VTB8 7 3>;>4C20==O4V ;V:C20==O <5B>?@>;>;< VA=CT@V2=O=> 7
;V:C20==O< =5A5;5:B82=8<8 □-1;>:0B>@0<8.
5B@>?@>;>; <>65 <0A:C20B8 45O:V ;;V=VG=V ?@>O28 B8@5>B>:A8:>7C (=0?@8::04, B0EV:0@4VN).
V7:0 2V4@8E =0 B8@5>B>:A8:>7 ?@>B8?>:070=0 G5@57 <>6;825 ?>A8;5==O A8<0B8:8.
0FVT=B8, O:V ?@>E>4OBL ;V:C20==O A5@F52>W =54>AB0B=>ABV, ?>28==V ?@>E>48B8 ;V:C20==O
4> ?>G0B:C 70AB>AC20==O <5B>?@>;>;C, 0 B0:>6 ?V4 G0A FL>3> ;V:C20==O.

C65 @V4:> 265 VA=CNGV ;53:V D>@<8 AV-?>@CH5==O ?@>2V4=>ABV <>6CBL >1BO6C20B8AO B0
?@872>48B8 4> AV-1;:>048 1V;LH BO6:>3> ABC?5=O. 0FVT=B8 7 AV-1;:>04>N ABC?5=O ?>28==V
?@>E>48B8 ;V:C20==O F8< ?@5?0@0B<< 4C65 >15@56=>.
>15@56=VABN <5B>?@>;>; 70AB>A>2C20B8 E2>@8< 7
28?04:C @>728B:C 1@048:0@4VW (!! <5=H5 50-55 C4/E2) C E>4V ;V:C20==O <5B>?@>;>;< 4>70 <0T
1CB8 7<5=H5=0 B0/01> ?@5?0@0B A;V4 ?>ABC?>2> 2V4
024O:8 A2>W9 3V?>B5=782=V9 4VW ?@5?0@0B <>65 ?>A8;8B8 ?@>O28 A8@CH5=L ?5@8D5@8G=>3>
:@>2>>1V3C, B0:8E O: ?5@5
/:I> ?@5?0@0B 70AB>A>2C20B8 ?0FVT=B0<, E2>@8< =0 D5>E@><>F8B> A;V4 70AB>A>2C20B8 α-A8
;VB8G=89 ?@5?0@0B.
/:I> =5>1EV4=> ?@8?8=8B8 ;V:C20==O V C 28?04:C, :>;8 F5 <>6;82>, 9>3> A;V4 ?@8?8=8B8 ?@>BO3<<
10-14 4=V2 7V I>45==8< 7=865==O< 4>78 =0 25 <3 =0 4>1C ?@>BO3>< >AB0==VE 6 4=V2. @>BO3<<
FL>3> ?5@V>4C >A>1;82C C203C ?>B@V1=> ?@84V;OB8 ?0FVT=B0< 7 VH5N E2>@>1>N A5@FO. 878:
28=8:=5==O A5@F528E =0?04V2, 2;:NG0NG8 @0?B>289 ;5B0;L=89 =0A;V4>;, <>65 71V;LHC20B8AO
?V4 G0A ?@8?8=5==O ;V:C20==O □-1;:>:0B>@0<8.
5B>?@>;>; <>65 A?@8G8=8B8 =57=0G=5 ?V428I5==O @V2=V2 B@83;VF5@84V2 B0 7<5=H5==O
@V2=V2 2V;L=8E 68@=8E :8A;>B C :@>2V. # 45O:8E 28?04:0E A?>AB5@V30;>AO =57=0G=5 7
<5=H5==O @V2=V2 ;V?>?@>B5W=V2 =87L:>W IV;L=>ABV ()), V 2>=> 1C;> 7=0G=><5=H8<
?>@V2=O=> 7 ?@89><< =5A5;5:B82=8E β₂-1;:>:0B>@V2. "8< =5 <5=H5 T 40=V, I> 2 >4=>A;V465=L
1C;> ?>:070=5 7=0G=5 7=865==O @V2=O 7030;L=>3> E>;5AB5@8=C ?VA;O ;V:C20==O <5B>?@>;>;<
?@>BO3>< :V;L:>E @>:V2.
54>AB0B=L> 4>A2V4C 70AB>AC20==O <5B>?@>;>;C E2>@8< V7 A5@F52>N =54>AB0B=VABN B0
B0:8<8 AC?CB=V<8 D0:B>@0<8: =5AB01V;L=0 A5@F520 =54>AB0B=VABL (NYHA IV); 3>AB@89
V=D0@:B :0@40 01> =5AB01V;L=0 AB5=>:0@4VO C ?>?5@54=V 28 4=V2; ?>@CH5==O DC=:FVW
=8@>: B0 ?5GV=:8; 2V: ?0FVT=B0 2V4 80 @>:V2 B0 <5=H5 40 @>:V2; 35<>48=0 28@065=V
70E2>@N20==O ;:0?0=V2; 3V?5@B@>DVG=0 >1AB@C:B82=0 :0@4V>?0BVO; ?V4 G0A 01> ?@>BO3<<
4 ?5@0B82=>3> 2B@CG0==O =0 A5@FV. V:C20==O B0:8E ?0FVT=V2 ?>28==V ?@>2>48B8 ;V:0@V
7V A?5FV0;L=8<8 =028:0<8 B0 4>A2V4>
?0FVT=V2 7V AB5=>:0@4VTN @8=F<5B0;0 G0AB>B0 B0 BO6:VABL =0?04V2 AB5=>:0@4VW<>65
71V;LH8B8AO 2=0A;V4>: >?>A5@54:>20=>3> α-@5F5?B>@0<8 72C65==O :>@>=0@=8E AC48=. ">
=5A5;5:B82=V β₁-1;:>:0B>@8, A5;5:B82=V β₁-1;:>:0B>@8 A;V4 70AB>A>2C20B8 7 >15@56=VABN.
=0DV;0:B8G=89 H>: BO6:> ?@>BV:0T C ?0FVT=V2, O:V ?@>E>4OBL ;V:C20==O □-1;:>:0B>@0<8.
0FVT=B8, 2 VAB>@VW E2>@>18 O:8E 1C;8 2V47=0G5=V BO6:V 0;5@3VG=V @50:FVW, ?>28==V
?@>E>48B8 ;V:C20==O <5B>?@>;>;< 4C65 >15@56=>. A>1;82C C203C B0:>6 A;V4 ?@84V;OB8
?0FVT=B0< 7 0;5@3VG=8<8 @50:FVO<8, O:V ?@>E>4OBL ;V:C20==O 20:F8=0<8 (45A5=A81V;V7CNG0
B5@0?VO). D5:B 2V4 22545==O 728G09=8E 4>7 04@5=0;V=C <>65 1CB8 2V4ACB=V
0FVT=B0<, O:V :>@8ABCNBLAO :>=B0:B=8<8 ;V=70<8, A;V4 2@0E>2C20B8, I> ?@5?0@0B <>65 7
<5=HC20B8 A5:@5FVN A;V7=>W @V48=8.
0FVT=B8 7 ?A>@V07>< 01> 45?@5A82=8<8 70E2>@N20==O<8 2 0=0<=57V ?>28==V ?@>E>48B8
;V:C20==O <5B>?@>;>;< BV;L:8 ?VA;O @5B5;L=>3> 282G5==O 2V4=>H5==O ?>78B82=>3> 5D5:BC 4>
@878:C.
0FVT=B0< 7 BO6:8<8 ?>@CH5==O<8 DC=:FVW =8@>;, 7 A5@9>7=8<8 3>AB@8<8 AB0=0<8, I>
AC?@>2>46CNBLAO <5B01>;VG=8< 0F84>7>< B0 ?0FVT=B0<, O:V >B@8<1V=>20=5 ;V:C20==O
?@5?0@0B0<8 =0?5@ABO=:8, A;V4 ?@84V;8B8 >A>1;82C C203C.
@5?0@0B 7C, B>3> =5 A;V4 ?@87=0G0B8 E2>@8< 7V A?04:>28< 45DVF8B>< ;0:B078, =5?5@5=>A878
01> ?>@CH5==O< <5B01>;V778/30;0:B>78.

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

5B>?@>;>;, O: V V=HV ;V:0@AL:V 70A>18, =5 A;V4 70AB>A>2C20B8 C ?5@V>4 203VB=>ABV 01>
3>4C20==O 3@C44N 157 :@09=L>W ?>B@518. /: V V=HV β-04@5=>1;:>:0B>@8, <5B>?@>;>; <>65
A?@8G8=8B8 ?>1VG=V 5D5:B8, B0:V O: 1@048:0@4VO B0 3V?>3;V:540 B0 =>2>=0@>465=>3> 01> C =5
<>2;OB8 C ?5@V>4 3@C4=>3> 3>4C20==O.

/: ?@028;>, β-1;>:0B>@8 ?@83=VGCNBL ?;0F5=B0@=89 :@>2>BV:, I><>65 AB0B8 ?@8G8=>N 70B@8
ABC ?;>40. 5B>?@>;> <>65 A?@8G8=8B8 @>728B>: 1@048:0@4VW, 0@B5@V0;L=>W 3V?>B5=7VW,
3V?>3;V:52>=0@>465=8E, B>3> ?@89>< A;V4 ?@8?8=8B8 70 48-72 3>48=8 4> >GV:C20=>3> ?>G0B:C
?>;>3V2. /:I> F5 =5<>6;82>, =5>1EV4=> @5B5;L=> :>=B@>;N20B8 AB0= =5<>2;OB8 ?@>BO3>< 48-72
3>48= ?VA;O =0@>465==O.
V=H>3> 1>;C, :V;L:VABL<5B>?@>;>;C, O:C =5<>2;O >B@8< 7 3@C4=8< <>;>:×, 4;O @50;V70FVW
?>B5=7V9=>3> 5D5:BC 1;>;C20==O β-04@5=>@5F5?B>@V2 T =57=0G=>N 70 C<>2, O:I> 4>78
<5B>?@>;>;C, O:V >B@84C20==V 4;O 28O2;5==O ?>B5=7V9=8E 5D5:BV2 β-1;>:048.

**40B=VABL 2?;820B8 =0 H284:VABL @50:FVW ?@8 :5@C20==V 02B>B@0=A?>@B× 01> V=H8<8
<5E0=V7<0<8. V4 G0A ;V:C20==O ?@5?0@0B× <>65 28=8:=CB8 70?0<>@>G5==O B0 AB>
<;N20=VABL. 0FVT=BV2, 4VO;L=VABL O:8E ?>2O70=0 7 =0?@C65==O× C2038, 0 A0<5: :5@C20==O
02B><>1V;5< B0 @>1>BV 7 <5E0=V7<0<8, A;V4 ?>?5@548B8 ?@> <>6;82VABL 28=8:=5==O B0:8E
5D5:BV2.**

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

5B>?@>;>; ?@87=0G5=89 4;O I>45==>3> ?@89> 7@0=:C. "01;5B:C A;V4 ?@89<0B8 =5 @>76>2CNG8,
70?820B8 4>AB0B=L>N :V;L:VABN ?8B=>W 2>48.# ?5@V>4 ?V41>@C 4>78 A;V4 :>=B@>;N20B8
G0AB>BC A5@F528E A:>@>G5=L 4;O ?>?5@5465==O 1@048:0@4VW. 0:A8<0;L=0 4>1>20 4>70 400 <3.
@B5@V0;L=0 3V?5@B5=7VO. 5:><5=4>20=0 4>70 AB0=>28BL 100 <3 (>4=>@07>2> 2@0=FV 01>
@>7?>4V;ONG8 =0 420 ?@89><8 2@0=FV B0 225G5@V). /:I> ?@8 B0:>7C20==V B5@0?52B8G=>3>
5D5:BC =5 4>AO3=CB>, 4>1>20 4>70 <>65 1CB8 71V;LH5=0 4> 200 <3 (>4=>@07>2> 2@0=FV 01>
@>7?>4V;ONG8 =0 420 ?@89><8 2@0=FV B0 225G5@V) 01> ?@5?0@0B A;V4 :><1V=C20B8 7 V=H8<8
0=B83V?5@B5=782=8<8 ?@5?0@0B0<8.

!B5=>:0@4VO. 5:><5=4>20=0 4>70 ?@5?0@0BC AB0=>28BL 50-100 <3 2-3 @078 =0 4>1C. # @07V
=5>1EV4=>ABV ?@5?0@0B <>6=0 :><1V=C20B8 7 V=H8<8 ?@5?0@0B0<8 4;O ;V:C20==O
AB5=>:0@4VW.

@8B 5:><5=4>20=0 4>70 AB0=>28BL 50 <3 2-3 @078 =0 4>1C. @8 =5>1EV4=>ABV 4>1>2C 4>7C
71V;LH8B8 4> 300 <3, @>7?>4V;5=C =0 2-3 ?@89><8.

@8 V=D0@:BV:0@40 (;V:C20==O 1060=> @>7?>G0B8 ?@>BO3>< ?5@H8E 12 3>48= ?VA;O ?>O28
I>;N 2 3@C4OE). 5:><5=4>20=0 4>70 AB0=>28BL 50 <3 :>6=V 6 3>48= ?@>BO3>< 48 3>48=, ?V4B@8
<5=4>20=0 4>1>20 4>70 200 <3, @>7?>4V;5=0 =0 420 ?@89><8. C@A ;V:C20==O =5 <5=H5 3-E
V?5@B8@5>7 (B8@5>B>:A8:>7). 5:><5=4>20=0 4>70 AB0=>28BL 50 <3 4 @078 =0 4>1C. @8
4>AO3=5==V B5@0?52B8G=>3> 5D5:BC 4>7C A;V4 ?>ABC?>2> 7<5=HC20B8.

@>DV;0:B8:0 =0?04V2 5:><5=4>20=0 4>1>20 4>70 AB0=>28BL 100-200 <3 =0 4>1C, @>7?>4V;5=0 =0 2
?@89><8.

0FVT=B8 7 ?>@CH5==O< DC=:FVW =8@>.: 5<0T ?>B@518 :>@83C20B8 4>7C.

0FVT=B8 7 ?>@CH5==O< DC=:FVW ?5GV=:8. >@83C20==O 4>78 (7<5=H5==O 4>78 <5B>?@>;>;C)
70728G09 =5>1EV4=5 4;O ?0FVT=BV2 7 >1<565=8<8 ?5GV=:>28<8 DC=:FVO<8 (=0?@8;:04, 4;O
?0FVT=BV2 7 F8@>7>< ?5GV=:8).

0FVT=B8 ;VB=L>3> 2V:C. 5<0T ?>B@518 :>@83C20B8 4>7C.

VB8. 0AB>AC20==O ?@5?0@0BC ?@>B8?>:070=> 4VBO<.

5@54>7C20==O.

!8<8: ?5@54>7C20==O <5B>?@>;>;> <>65 ?@8725AB8 4> A8;L=>3> 7=865==O 0@B5@V0;L=>3>
B8A:C, A8=CA>2>W 1@048:0@4VW, 0=B@V>25=B@8:C;O@=>W 1;>:048 -ABC?5=O, ?>4>265==O
V=B5@20;C QT, 0A8AB>;VW, =54>AB0B=L>W ?5@8D5@8G=>W ?5@DC7VW, A5@F52>W
=54>AB0B=>ABV, :0@4V>35==>3> H>;C, 7C?8=:8 A5@FO, 1@>=E>A?077C?8=:8 48E0==O,
?V428I5=>W AB>;N20=>ABV, ?>@CH5==O 01> 2B@0B8 A2V4><>ABV, 4@V1=>@>7<0H8AB>E>4C,
3V?>3;V:5A>1;82> C 4VB59), 3V?5@3;V:57C, 3V?>:0;VTABV A2V4><>ABV, =530B82=>2>3> 3> A8=4@>
!C?CB=T 26820==O 0;>3>;N, ?@89>< 0=B83V?5@B5=782=8E ?@5?0@0BV2, EV=V48=C 01>
10@1VBC@0BV2 <>6CBL ?>3V@H8B8 AB0= ?0FVT=B0. 5@HV >7=0:8 ?5@54>7C20==O <>6CBL
28=8:=CB8 G5@57 20 E28;8= 2 3>48=8 ?VA;O ?5@54>7C20==O.
V:C20==O ?@>2>48BLAO 2 C<>20E 2V44V;5==O V=B5=A82=>W B5@0?VW.@89>< 0:B82>20=>3>

2C3V;;O,C @07V =5>1EV4=>ABV ?@<<820=O H;C=:0. # 28?04:C 206:8E D>@< 3V?>B5=7VW,
1@048:0@4VW 01> 703@>78 A5@F52>W =54>AB0B=>ABV A;V4 22>48B8 β₁-03>=VAB
2=CB@VH=L>25==> (=0?@8;:04, ?@5=0;B5@>;) 7 V=B5@20;>< 2-5 E28;8= 01> V=DC7V9=> 4>
4>AO3=5==O B5@0?52B8G=>3> 5D5:BC. # @07V 2V4ACB=>ABV A5;5:B82=>3> β₁-03>=VAB0<>6=0
22>48B8 2=CB@VH=L>25==> 4>?0 0B@>?V=C AC;LD0B 4;O 1;>:048 1;C:0NG>3> =5@20. B@>?V=
(0,25-0,5<3 4>@>A;8<, 10-20 65 7=04>18B8AO V=BC10FVO B0 28:>@8AB0==O 0?0@0BC HBCG=>3>
48E0==O; 045:20B=5 2V4=>2;5==O >1TW :@>2V; V=DC7VO 3;N:>78;<=>VB>@C20==O ; ?>2B>@=5
2=CB@VH=L>25==5 22545==O 0B@>?V=C 1-2<3 (3>;>2=8< G8=>< ?@8 203CA=8E A8<0E). /:I>
B5@0?52B8G=>3> 5D5:BC =5 4>AO3=CB>, <>6=0 28:>@8AB0B8 V=HV A8=>@04@5=0;V=.
"0:>6 A;V4 22>48B8 3;N:03>= C 4>7V 50-150<:3/:3<0A8 BV;0 2=CB@VH=L>25==>, 0 B0:>6 0<@8=>=.
@8 7=0G=V9 1@048:0@4VW, @5D@0:B5@=V9 4><548:0<5=B>7=>W B5@0?VW =5>1EV4=> 70AB>A
>2C20B8 HBCG=89 2>4V9 A5@F52>3> @8BV@C20==O 1@>=E>A?0748B8 2=CB@VH=L>25==> β₂-
03>=VAB. !;V4 2@0E>2C20B8, I> 4>78 0=B84>BV2, =5>1EV4=V 4;O CAC=5==O A87C20==O β-
1;>:0B>@0<8, =01030B> 28IV 70 B5@0?52B8G=V, >A:V;L:8 β-@5F5?B>@8 72O70=V β-1;>:0B>@0<8.
">:A8G=VABL. # 4>@>A;>W ;N48=8 ?@89< 4>78 7,5 3 A?@8G8=O2 ;5B0;L=C V=B>:A8:0FVN. @89<
100<3 ?@5?0@0BC 5-@VG=>N 48B8=>N =5 AC?@>2>46C202AO A8<0<8 V=B>:A8:0FVW ?VA;O
?@>2545==O ?@><820==O H;C=:0. >:A8:0FVN A?@8G8=8;0 4>70 450<3 C 12-@VG=>W 48B8=8 B0 4>70
2,5 3, 0 7,5 3 4C65 A5@9>7=C V=B>:A8:0FVN.
5>1EV4=89 ?8;L=89 =03;O4 70 ?0FVT=B>< (?0@0<5B@8 :@>2>>1V3C V 48E0==O, DC=:FVO =8@>:,
@V25=L 3;N:>78, 5;5:B@>;VB8 A8@>20B:8 :@>2V).
@07V ?@83=VG5==O DC=:FVW :0@40: V=DC7VO 4>1CB0 4>1CB0=0BC 9<3/<;, 10-20<;.

>1VG=V@50:FVW.

I>:C :@>2V B0 ;VW A8AB5<8: B@><1>F8B>?5=VO, 03@0=C;>F8B>7, ;59:>?5=VO.
5B0I>;VG=V B0 0;V<5=B0@=V @>7;048: 71V;LH5==O<0A8 BV;0.
I>:C ?A8EV:8: ?>@CH5==O A=C, A>;:82VABL, 157A>==O, =VG=V :>Hk0@8, 45?@5AVO, @>7;04
:>=F5=B@0FVW C2038, @>7;048 ?0<'OBV, 0<=57VO, A?;CB0=VABL A2V4<>ABV, 30;NF8=0FVW,
=5@2>7=VABL, B@82>6=VABL.
I>:C =5@2>2>W A8AB5<8: 70?0<>@>G5==O, 3>;>2=89 1V;L, ?0@5AB57VO, ?>@CH5==O A<0:>28E
2V4GCBV2.
I>:C >@30=V2 7>@C: ?>@CH5==O 7>@C, ACEVABL 2>G0E 01> 70?0;5==O :>='N=:B828.
I>:C >@30=V2 A;CEC B0 @V2=>2038: 2V4GCBBO HC=C C 2CE0E, ?>@CH5==O A;CEC.
I>:C A5@FO: ?>ABC@0;L=V ?>@CH5==O (4C65 @V4:> V7 70?0<>@>G5==O<), E>;>4=V :V=FV2:8,
1@048:0@4VO, 0B@V>25=B@8:C;O@=0 1;>:040 , 01> ABC?5=O, 1V;L C ?5@8:0@4V, 1V;L C 3@C4=V9
;;VBFV, <8=CI5 ?>A8;5==O A8<0B8:8 A5@F52>W =54>AB0B=>ABV, B0EV:0@4VO, 0@8B@CH5==O
A5@F52>W ?@>2V4=>ABV, 0@B5@V0;L=0 3V?>B5=7VO, :0@4V>35==89 H>: C ?0FVT=BV2 7 3>AB@8
<V=D0@:B>< :0@40, ?>A8;5=5 A5@F518BBO.
I>:C AC48=: >@B>AB0B8G=0 0@B5@V0;L=0 3V?>B5=7VO (I> 2 4C65 @V4:VA=8E 28?04:0E
AC?@>2>46CTBLAO A8=:>?5), A8=4@< 59=>, 30=3@5=0 C ?0FVT=BV2 7 =0O2=8<8 206:8<8
?>@CH5==O<8 ?5@8D5@8G=>3> :@>2>>1V3C.
I>:C @5A?V@0B>@=>W A8AB5<8, 3@C4=>W ;:VB:8 B0 A5@54>ABV==O: 7048H:0 ?@8 DV78G=>
=E>A?07<, @8=VB.
I>:C H;C=:>2>-.8H:>2>3> B@0:BC: =C4>B0, 1;N20==O, 1V;L C 682>BV, 4V0@5O, 70?>@, ACEVABL C
@>BV, ?5GVO, 74CBBO.
I>:C 35?0B>1V;V0@=>W A8AB5<8: 35?0B8B.
I>:C H:V@8 B0 ?V4H:V@=>W ;:VB:>28=8: @50:FVW 3V?5@GCB;82>ABV, 2;;NG0NG8 28A8?0==O (C
D>@@V0B8G=8E B0 48AB@>DVG=8E C@065=L H:V@8), :@>?82O=:C, A25@1V6, 5@8B5
B>GCB;82VABL, ?A>@V07, ?>A8;5==O 206:>ABV ?5@51V3C ?A>@V07C, ?>A8;5=0 ?VB;82VABL,
28?040==O 2>;>AAO; ?>@CH5==O 68@>2>3> >1
I>:C >?>@=>-@CE>2>3> 0?0@0BC B0 A?>;CG=>W B:0=8=8: <'O7>2V A?07<8, 0@B@0;3VO,
?>A8;5==O A8W :C;L302>ABV, <O7>20 A;01:VABL.
I>:C @5?@>4C:B82=>W A8AB5<8 B0 <>;>G=8E 70;>7: VB5=FVO/AB0B520 48ADC=:FVO, E2>@>10
59@>=V.
030;L=V @>7;048 B0 @50:FVW C : ?V428I5=0 2B><;N20=VABL, ?5@8D5@8G=V =01@O:8.

01>@0B>@=V ?>:07=8:8: 2V4E8;5==O 2V4 =>@<8 7 1>:C ?>:07=8:V2 DC=:FVW ?5GV=:8, ?>O20
0=B8=C::50@=8E 0=B8BV; (=5 ?>2O70=8E V7 A8AB5<=8< G5@2>=8< 2>2G0:><), 7=865==O @V2=O
E>;5AB5@8=C ;V?>?@>B5W4V2 28A>:>W IV;L=>ABV ()) V ?V428I5==O @V2=O B@83;VF5@84V2
?@8 =>@<0;L=>3> E>;5AB5@8=C.
5B>?@>;> <65 <0A:C20B8 A8<8 B8@5>B>:A8:>7C, ?@>O28 ;0B5=B=>3> FC:@>2>3> 4V015BC.

"5@ABV. 5 @>:V2.

#<>28 715@V30==O. 15@V30B8 2 >@83V=0;L=V9 C?0:>2FV ?@8 B525 °!. 15@V30B8 2 =54>ABC?=> .

#?0:>2:0. > 10 B01;5B>: C 1;VAB5@V. 31;VAB5@8 2 ?0GFV.

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

8@>1=8:. " «8W2<54?@5?0@0B».

VAf57=0E>465==O 28@>1=8:0 B0 9>3> 04@5A020465==O 4VO;L=>ABV. #:@0W=0, 01032, <. 8W2,
2C;.!0:A030=AL:>3>, 139.